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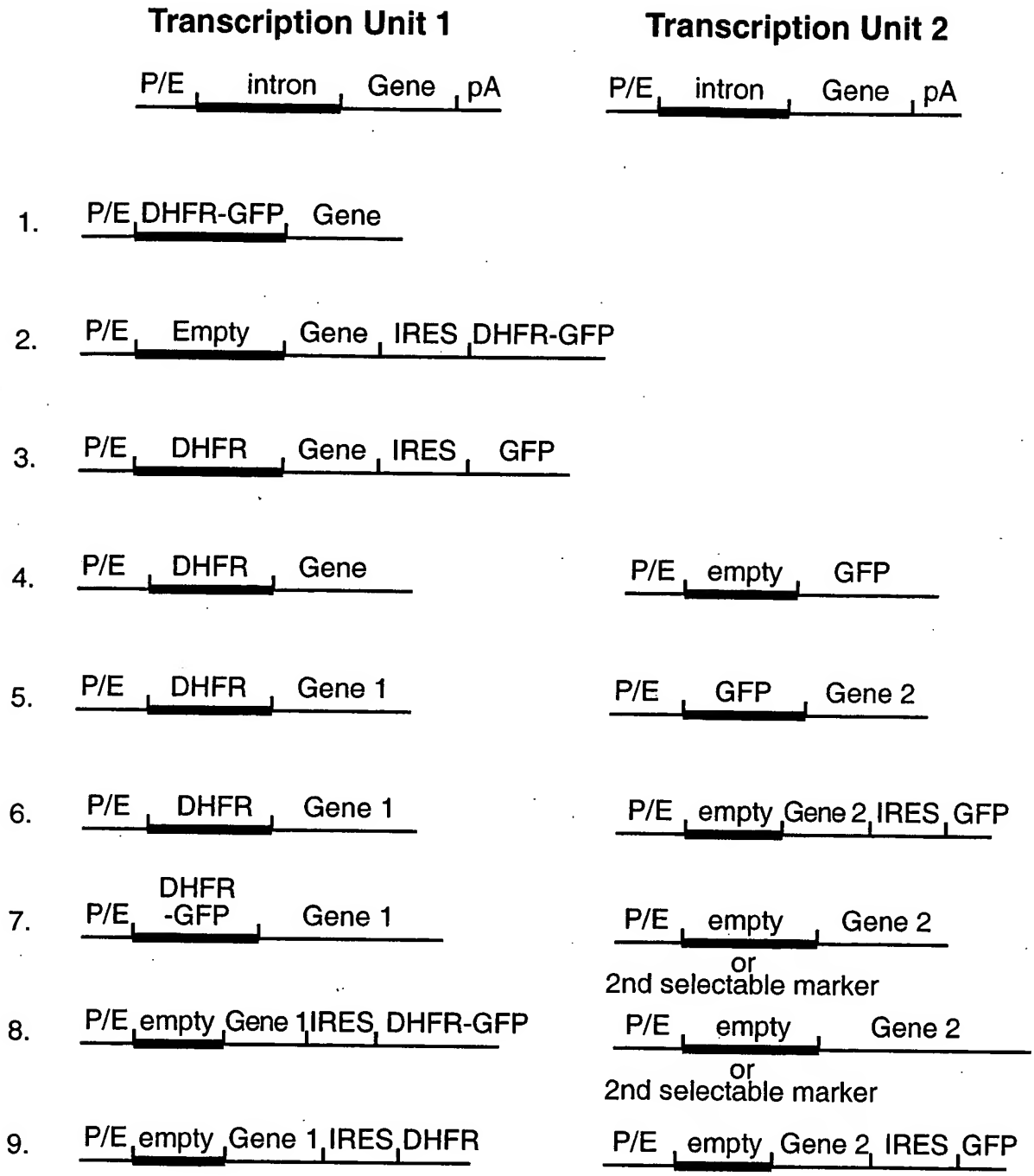

Transcription Unit 1
Transcription Unit 2
P/E intron Gene pA
P/E intron Gene pA
1. P/E DHFR-GFP Gene
2. P/E Empty Gene IRES DHFR-GFP
3. P/E DHFR Gene IRES GFP
4. P/E DHFR Gene
P/E empty GFP
5. P/E DHFR Gene 1
P/E GFP Gene 2
6. P/E DHFR Gene 1
P/E empty Gene 2 IRES GFP
7. P/E DHFR -GFP Gene 1
P/E empty Gene 2
or
2nd selectable marker
8. P/E empty Gene 1 IRES DHFR-GFP
P/E empty Gene 2
or
2nd selectable marker
9. P/E empty Gene 1 IRES DHFR
P/E empty Gene 2 IRES GFP

FIG._1

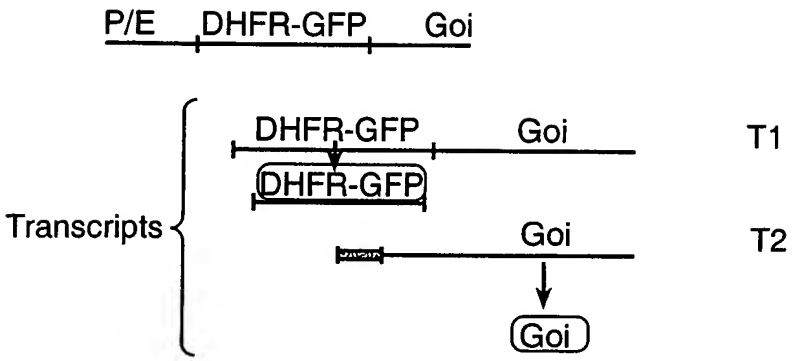


FIG._2A

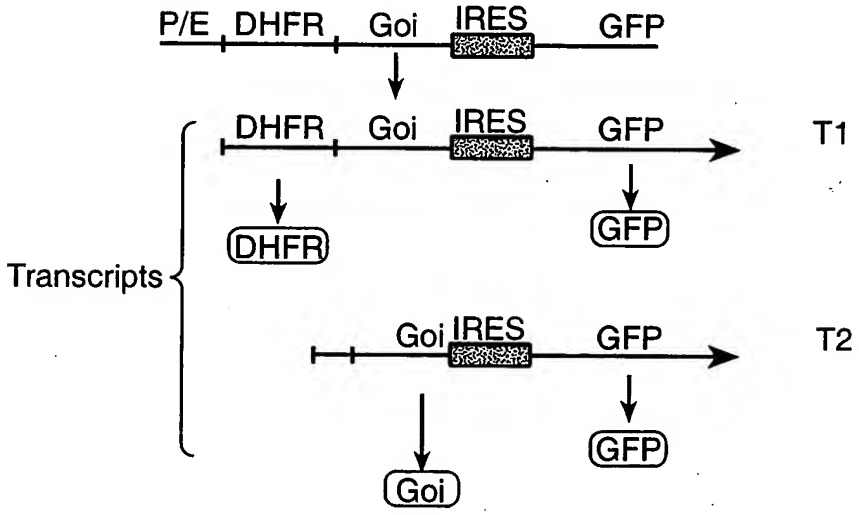


FIG._2B

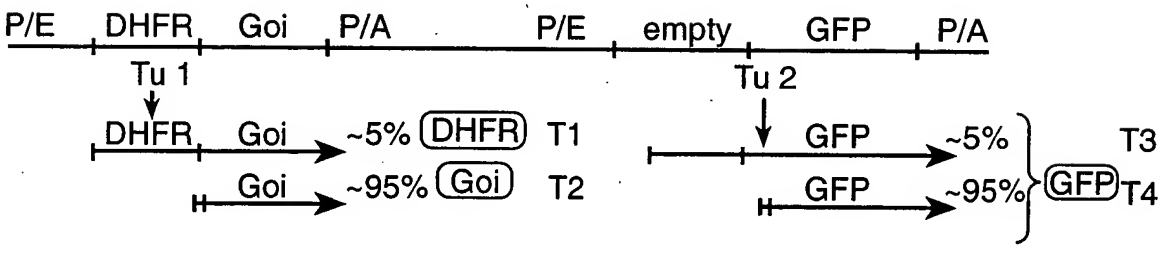


FIG._2C

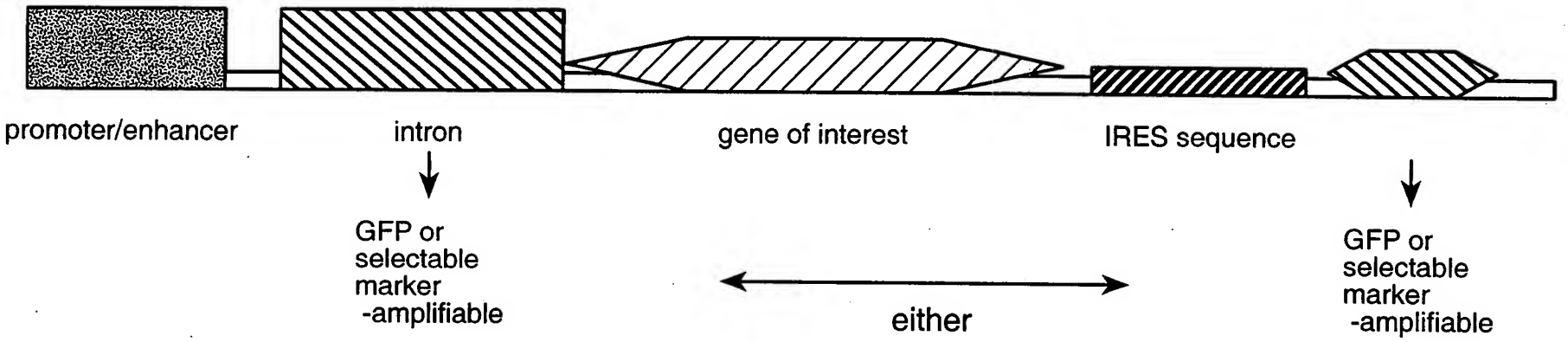

promoter/enhancer
intron
gene of interest
IRES sequence
GFP or
selectable
marker
-amplifiable
either
GFP or
selectable
marker
-amplifiable

FIG._3

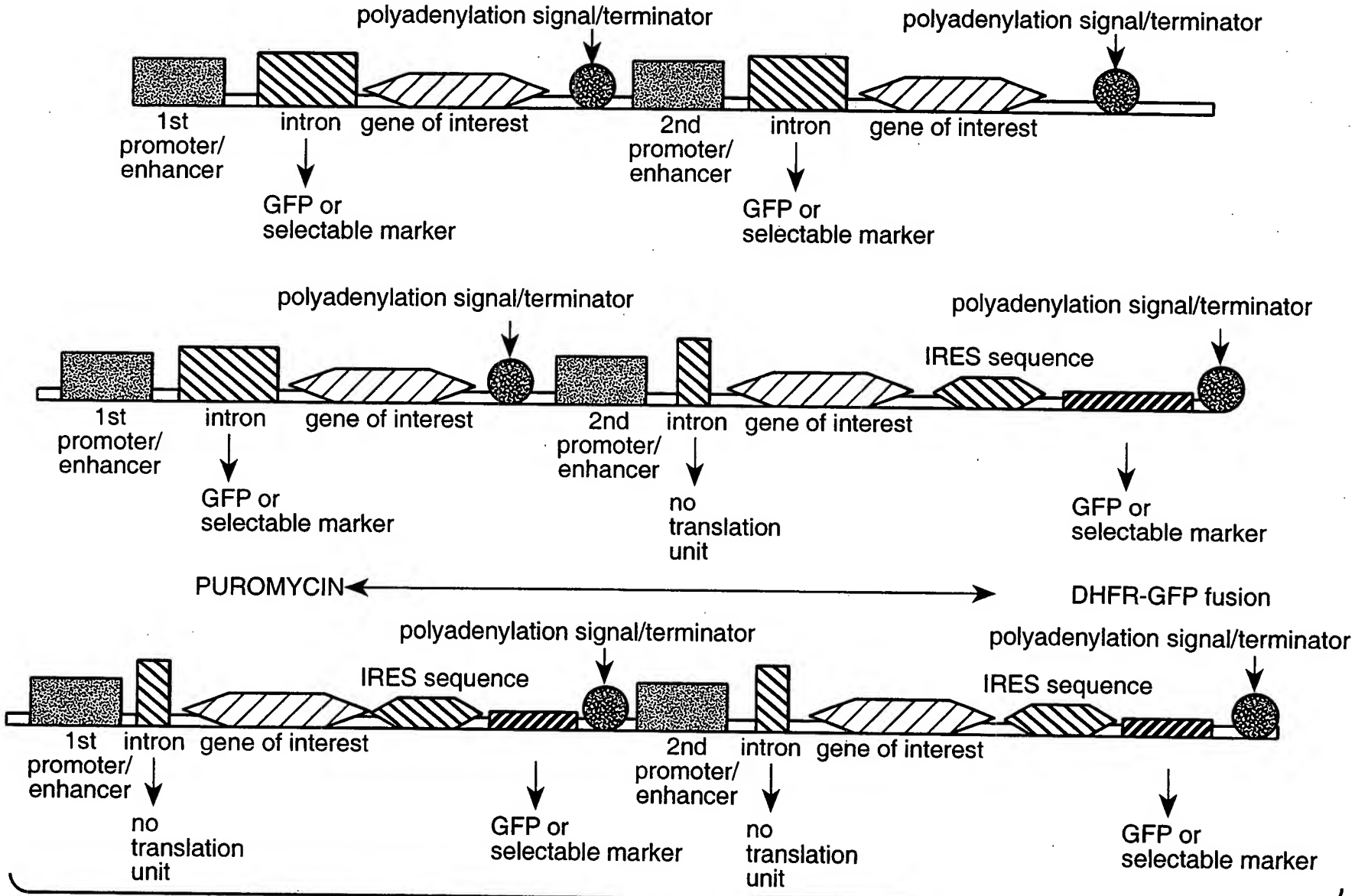

polyadenylation signal/terminator
polyadenylation signal/terminator
1st promoter/ enhancer
intron
gene of interest
2nd promoter/ enhancer
intron
gene of interest
GFP or selectable marker
GFP or selectable marker
polyadenylation signal/terminator
polyadenylation signal/terminator
IRES sequence
1st promoter/ enhancer
intron
gene of interest
2nd promoter/ enhancer
intron
gene of interest
GFP or selectable marker
no translation unit
GFP or selectable marker
PUROMYCIN
DHFR-GFP fusion
polyadenylation signal/terminator
polyadenylation signal/terminator
IRES sequence
IRES sequence
1st promoter/ enhancer
intron
gene of interest
2nd promoter/ enhancer
intron
gene of interest
no translation unit
GFP or selectable marker
no translation unit
GFP or selectable marker

FIG._4

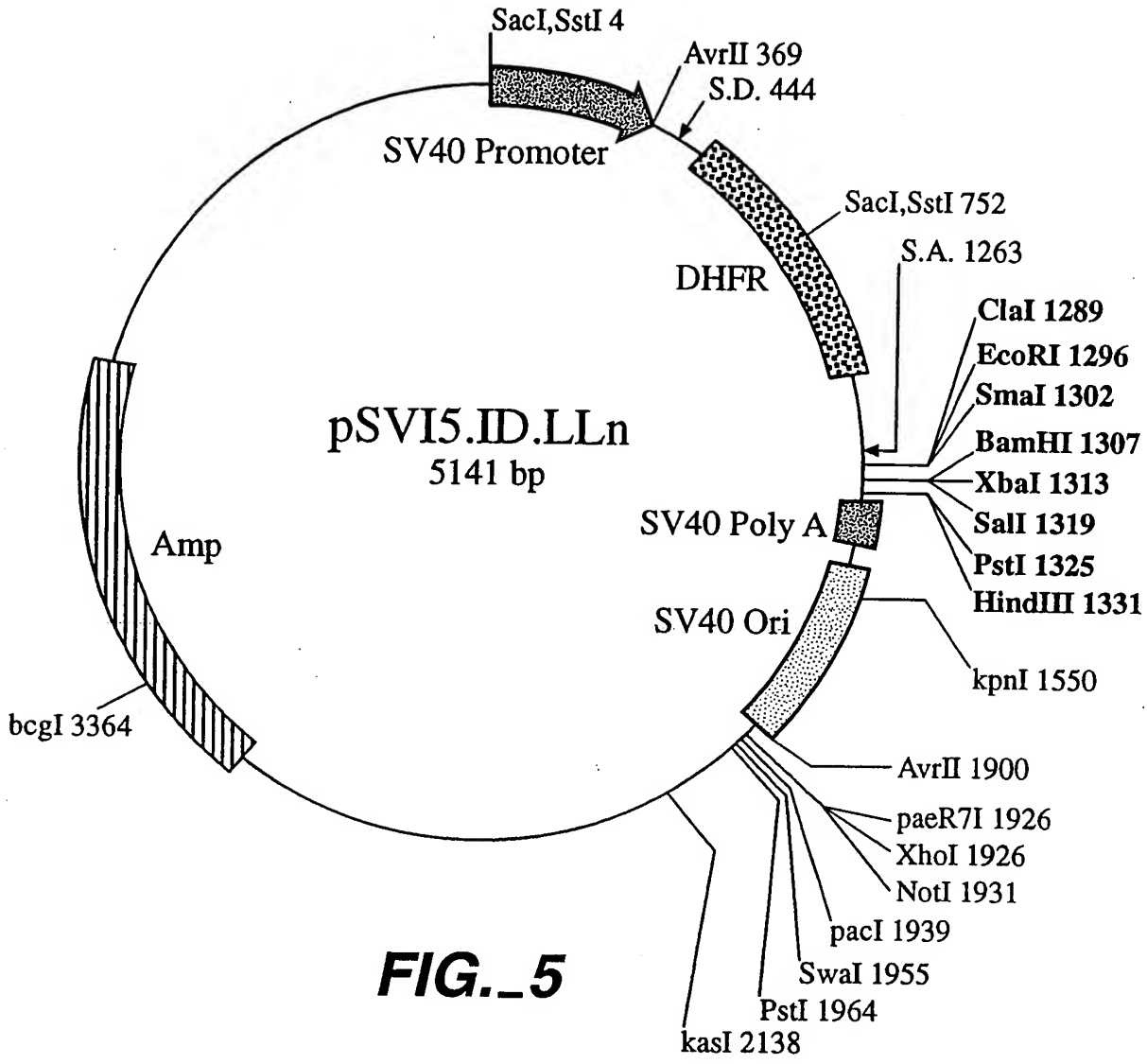

SacI,SstI 4
AvrII 369
S.D. 444
SV40 Promoter
SacI,SstI 752
S.A. 1263
DHFR
ClaI 1289
EcoRI 1296
SmaI 1302
BamHI 1307
XbaI 1313
SalI 1319
PstI 1325
HindIII 1331
pSVI5.ID.LLn
5141 bp
SV40 Poly A
Amp
SV40 Ori
kpnI 1550
bcgI 3364
AvrII 1900
paeR7I 1926
XhoI 1926
NotI 1931
pacI 1939
SwaI 1955
PstI 1964
kasI 2138

FIG._5

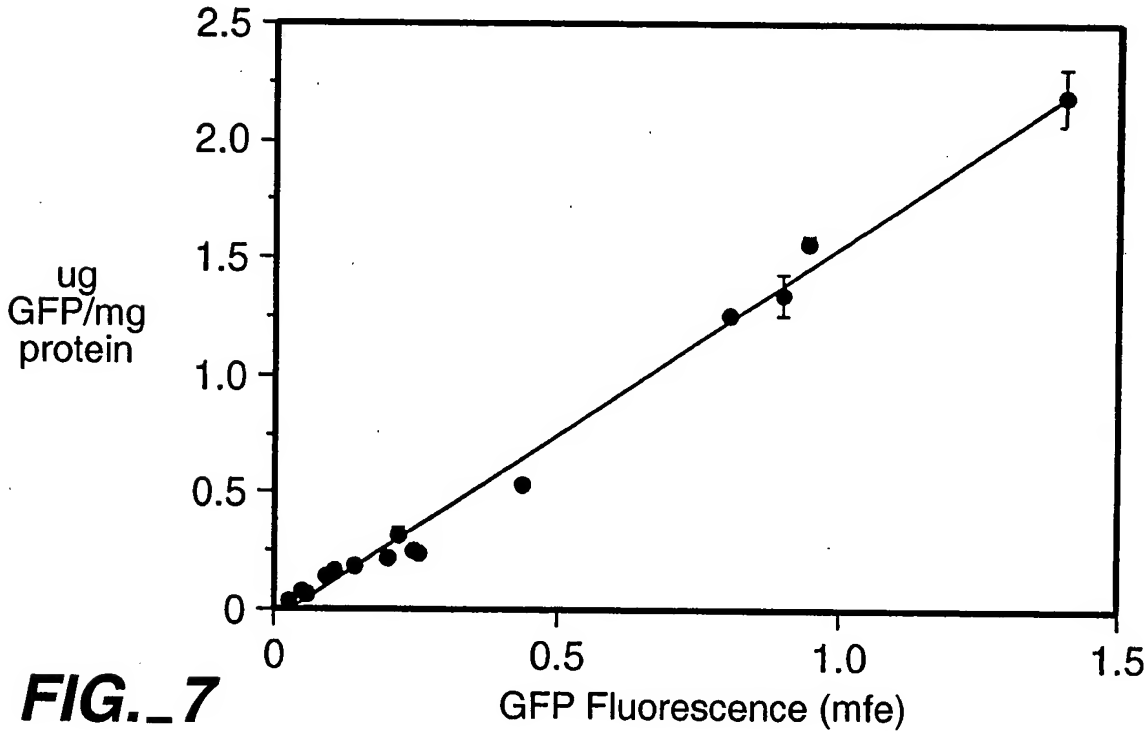

2.5
2.0
1.5
1.0
0.5
0
ug GFP/mg protein
0
0.5
1.0
1.5
GFP Fluorescence (mfe)

FIG._7

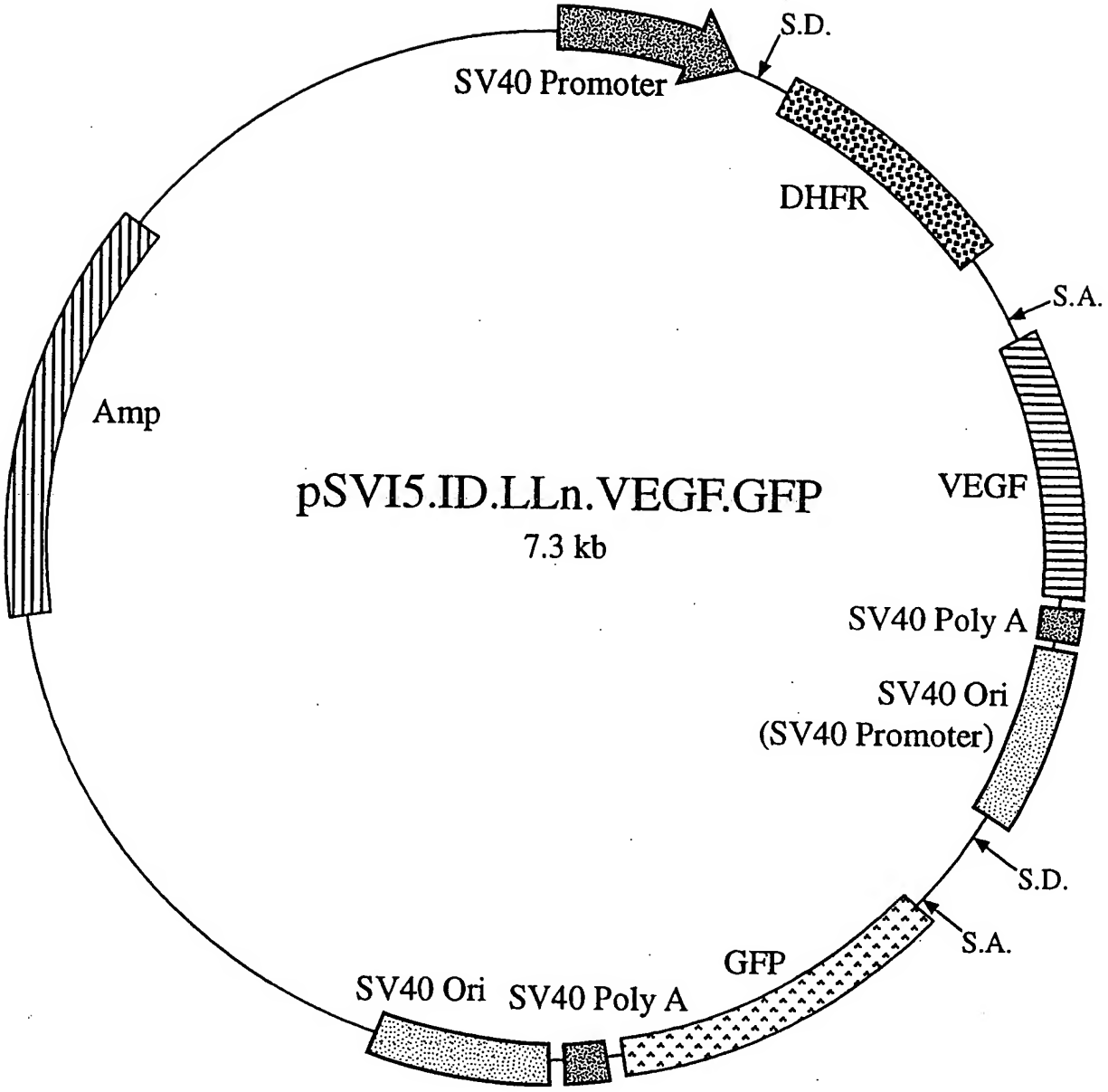

S.D.
SV40 Promoter
DHFR
S.A.
Amp
pSVI5.ID.LLn.VEGF.GFP
7.3 kb
VEGF
SV40 Poly A
SV40 Ori
(SV40 Promoter)
S.D.
S.A.
GFP
SV40 Ori
SV40 Poly A

FIG._6

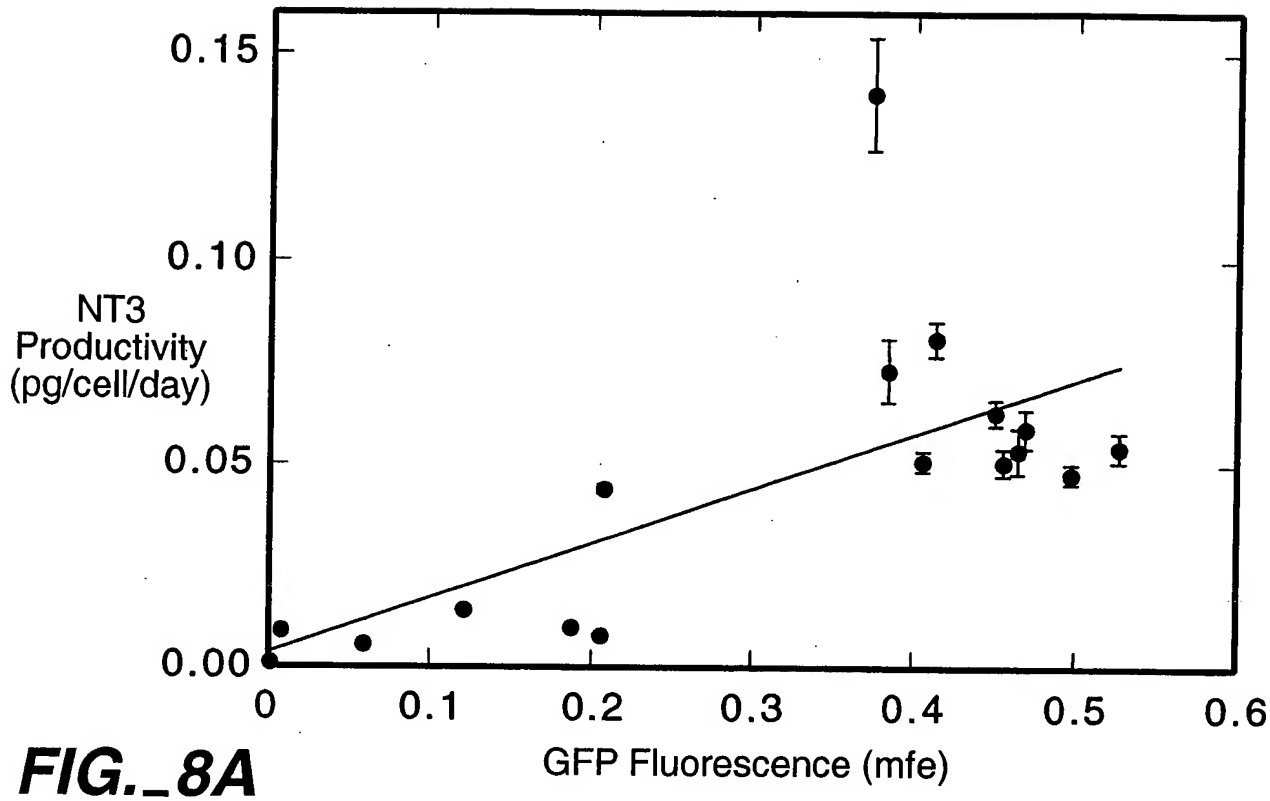

0.15
0.10
0.05
0.00
NT3
Productivity
(pg/cell/day)
0
0.1
0.2
0.3
0.4
0.5
0.6
GFP Fluorescence (mfe)

FIG._8A

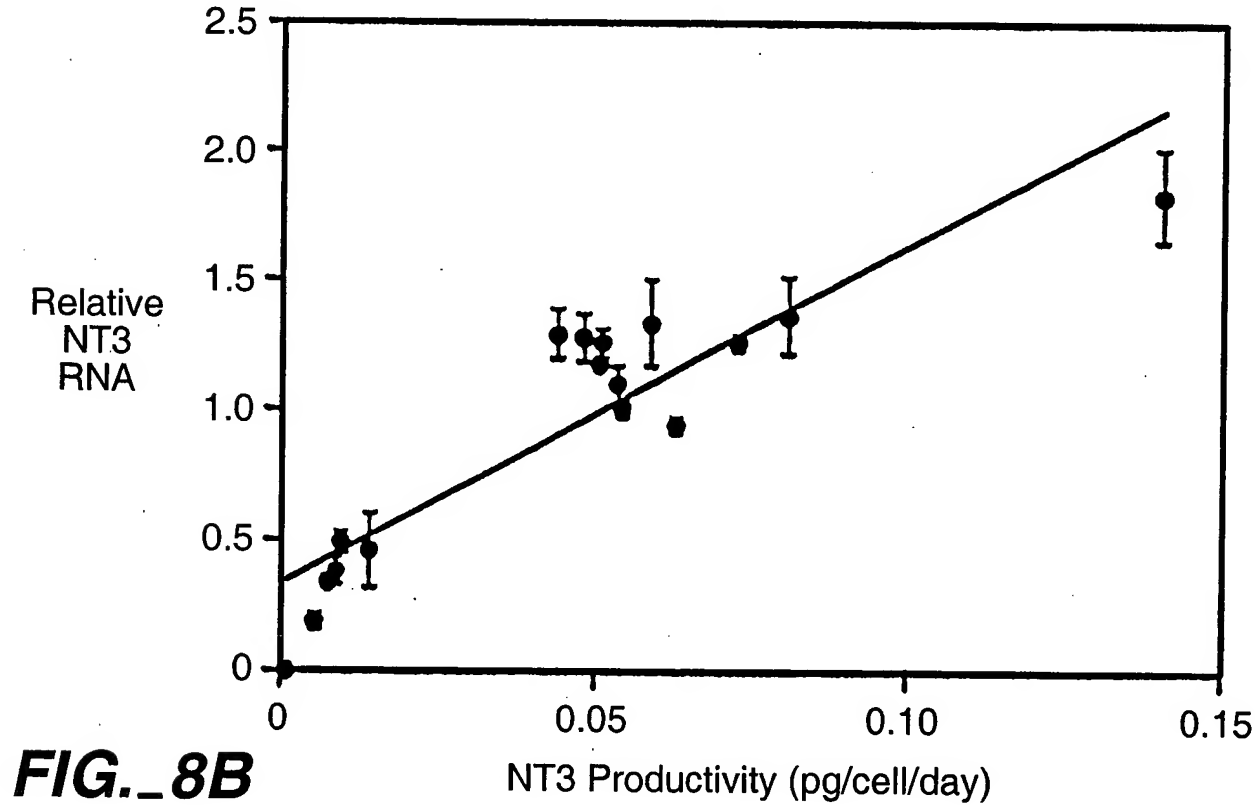

2.5
2.0
1.5
1.0
0.5
0
Relative
NT3
RNA
0
0.05
0.10
0.15
NT3 Productivity (pg/cell/day)

FIG._8B

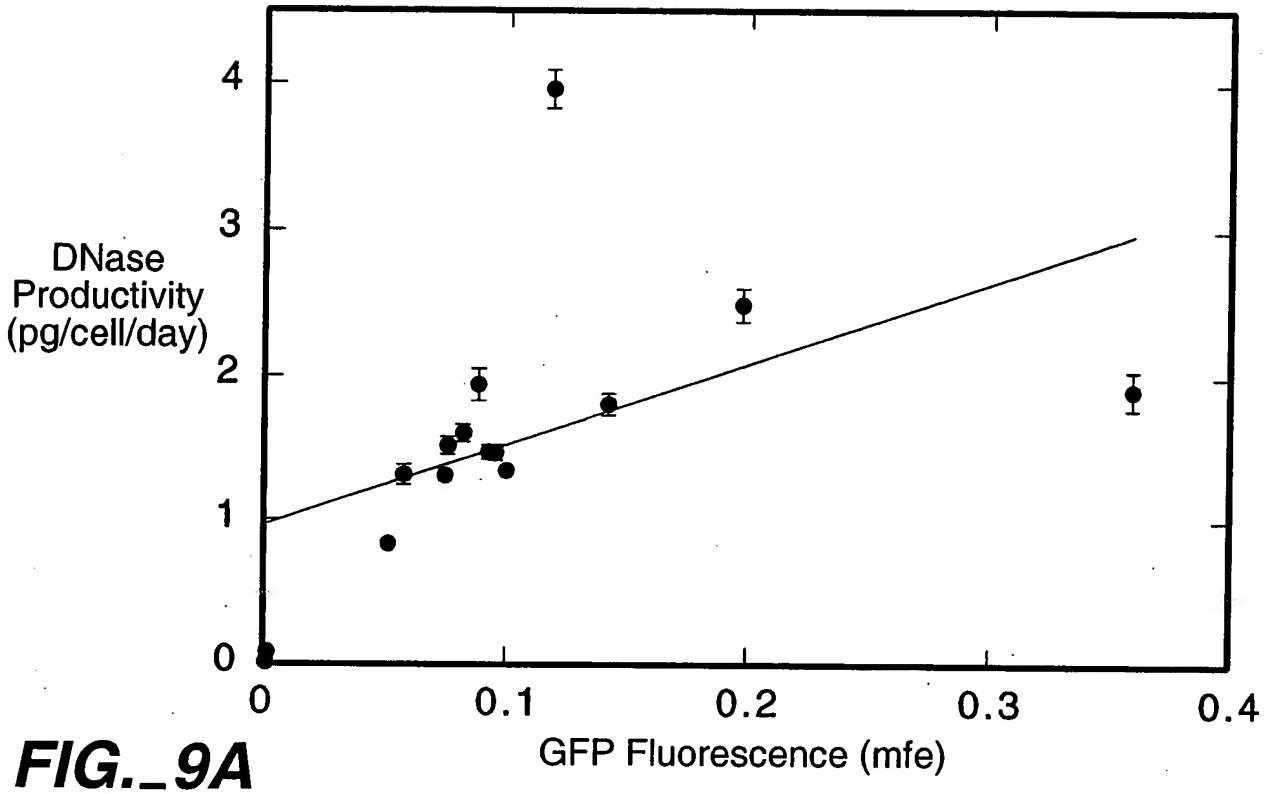

DNase
Productivity
(pg/cell/day)
4
3
2
1
0
0
0.1
0.2
0.3
0.4
GFP Fluorescence (mfe)

FIG._9A

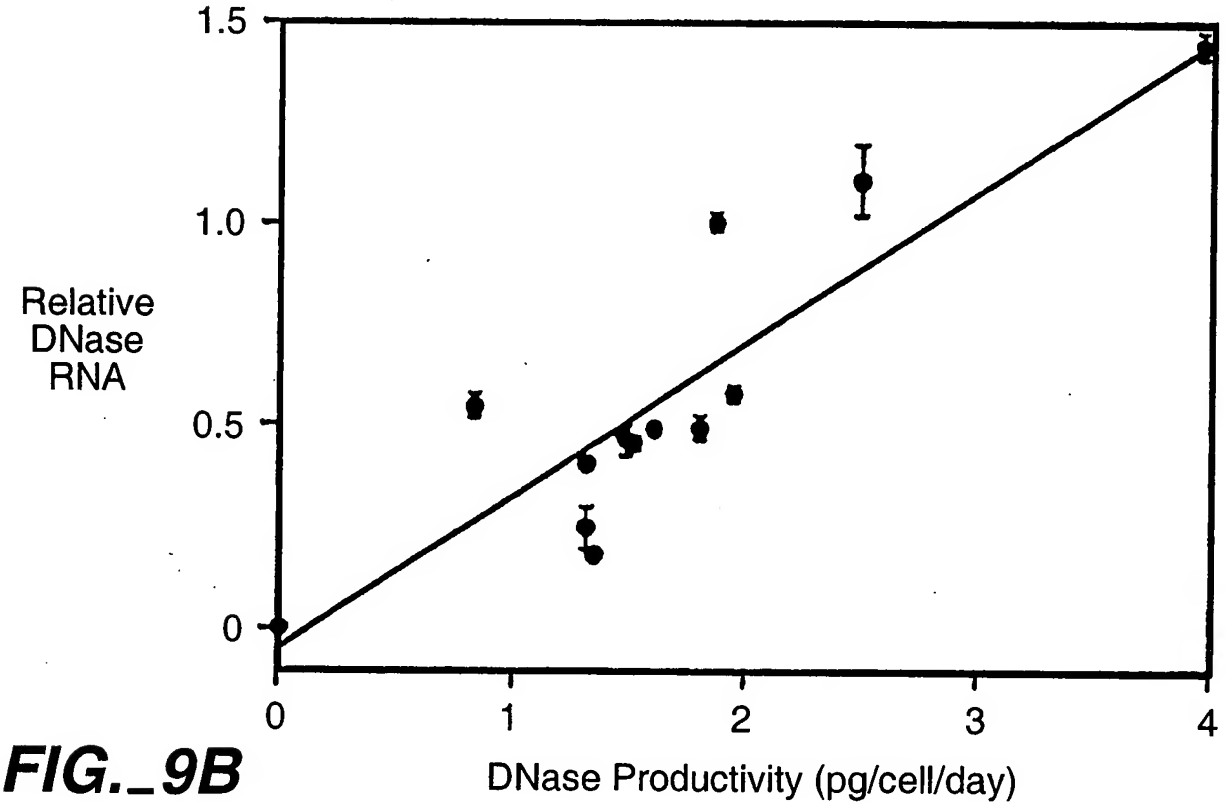

Relative
DNase
RNA
1.5
1.0
0.5
0
0
1
2
3
4
DNase Productivity (pg/cell/day)

FIG._9B

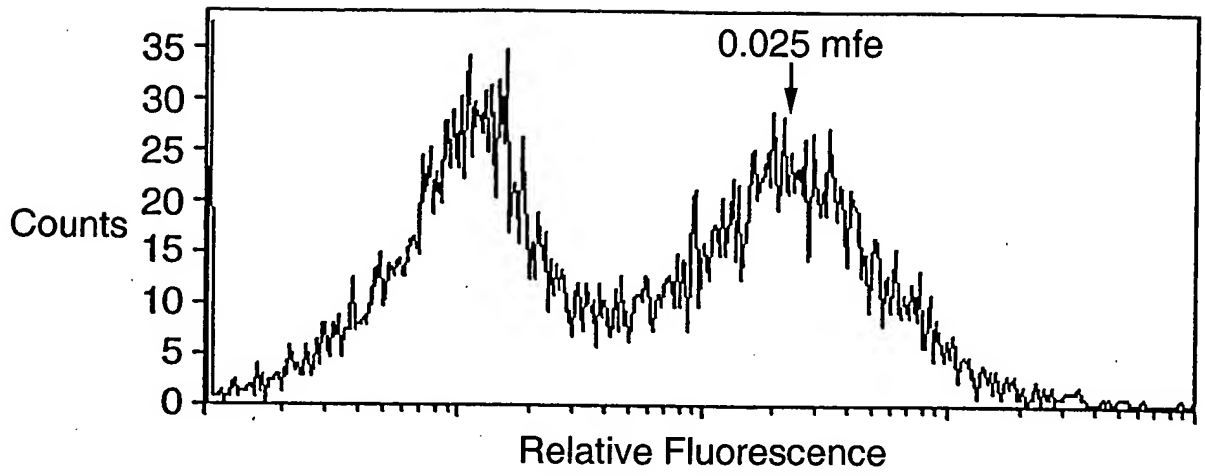


FIG._10A

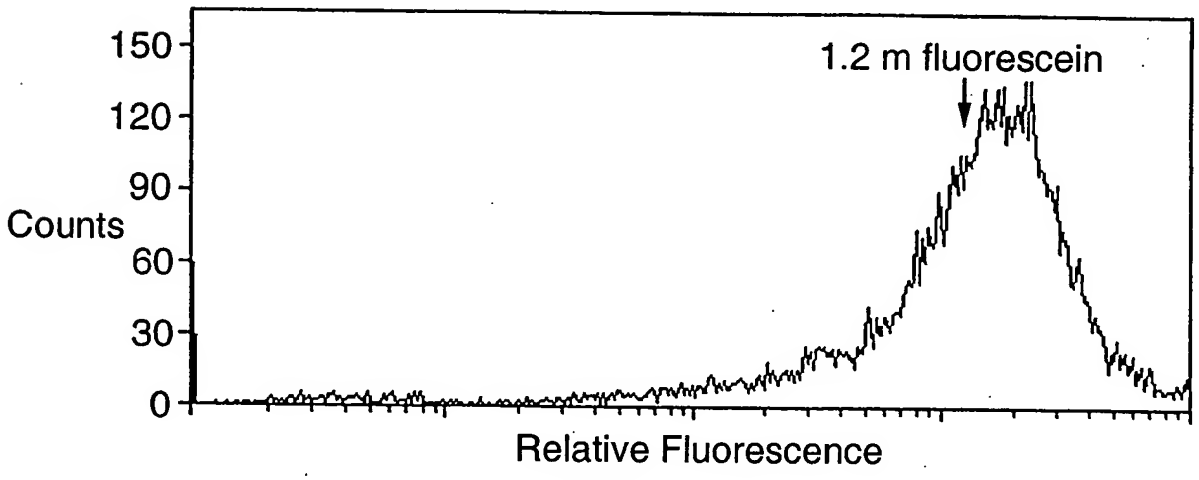


FIG._10B

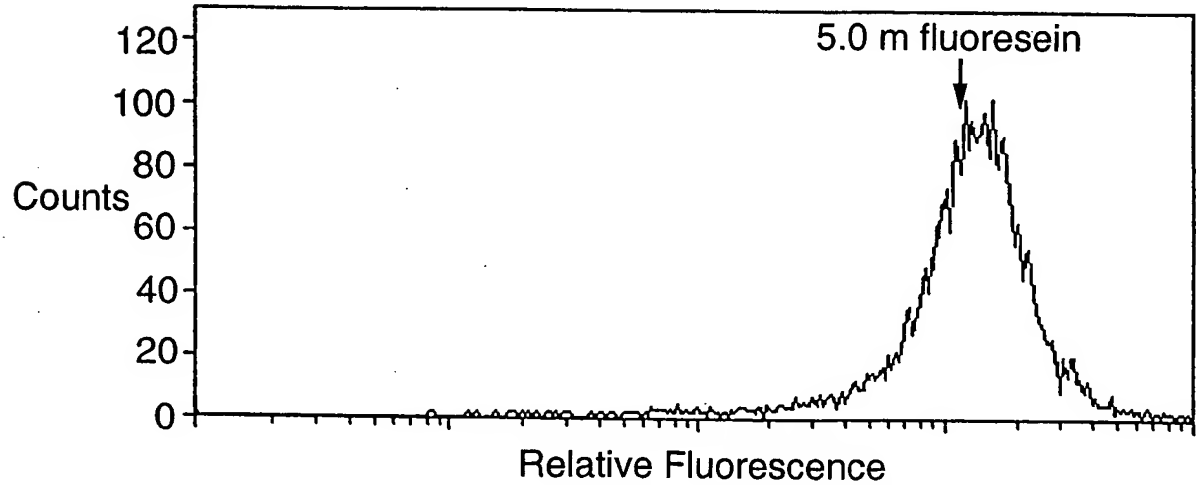


FIG._10C

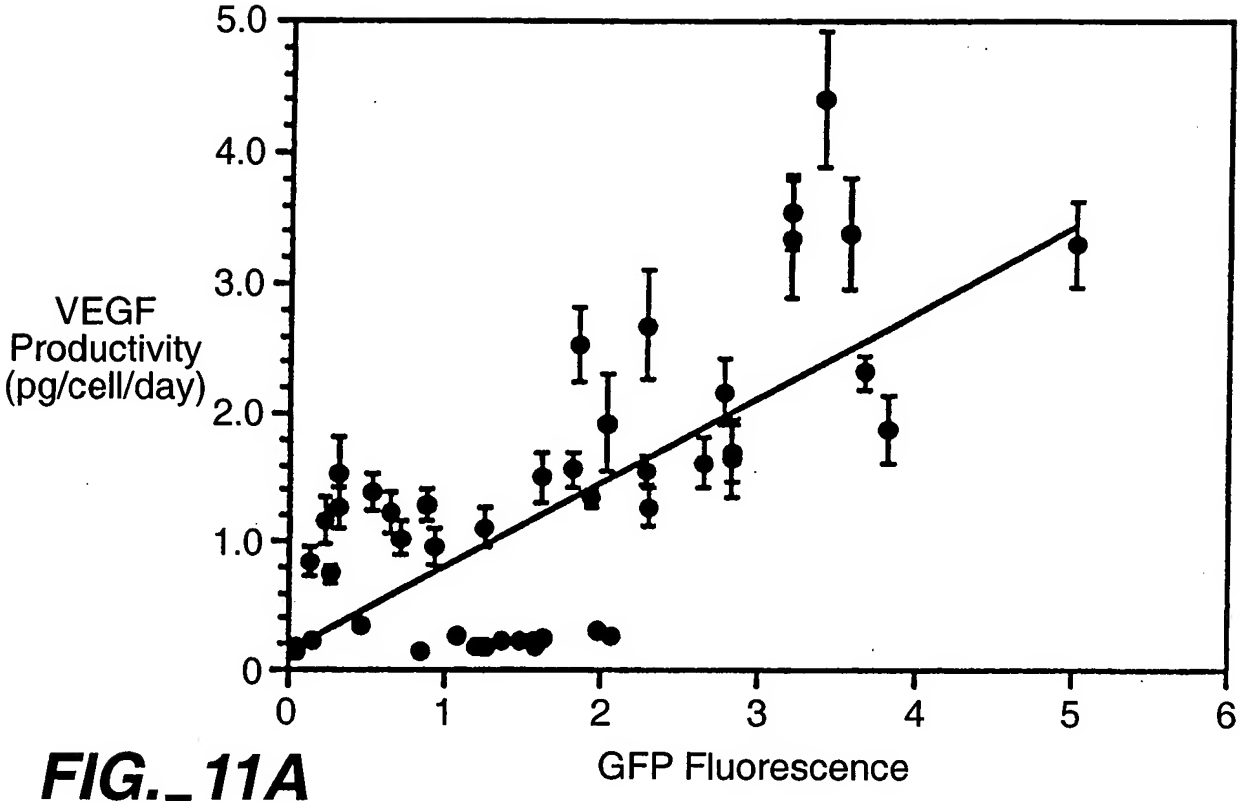


FIG._11A

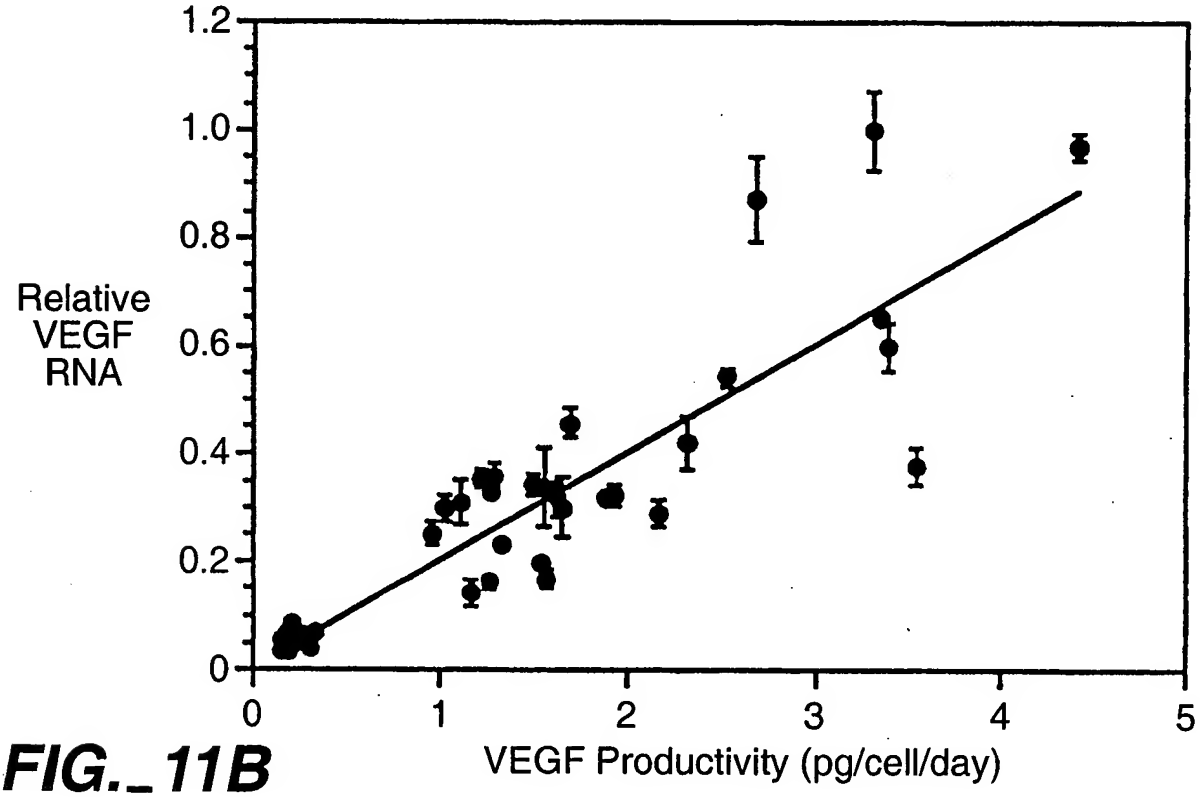


FIG._11B

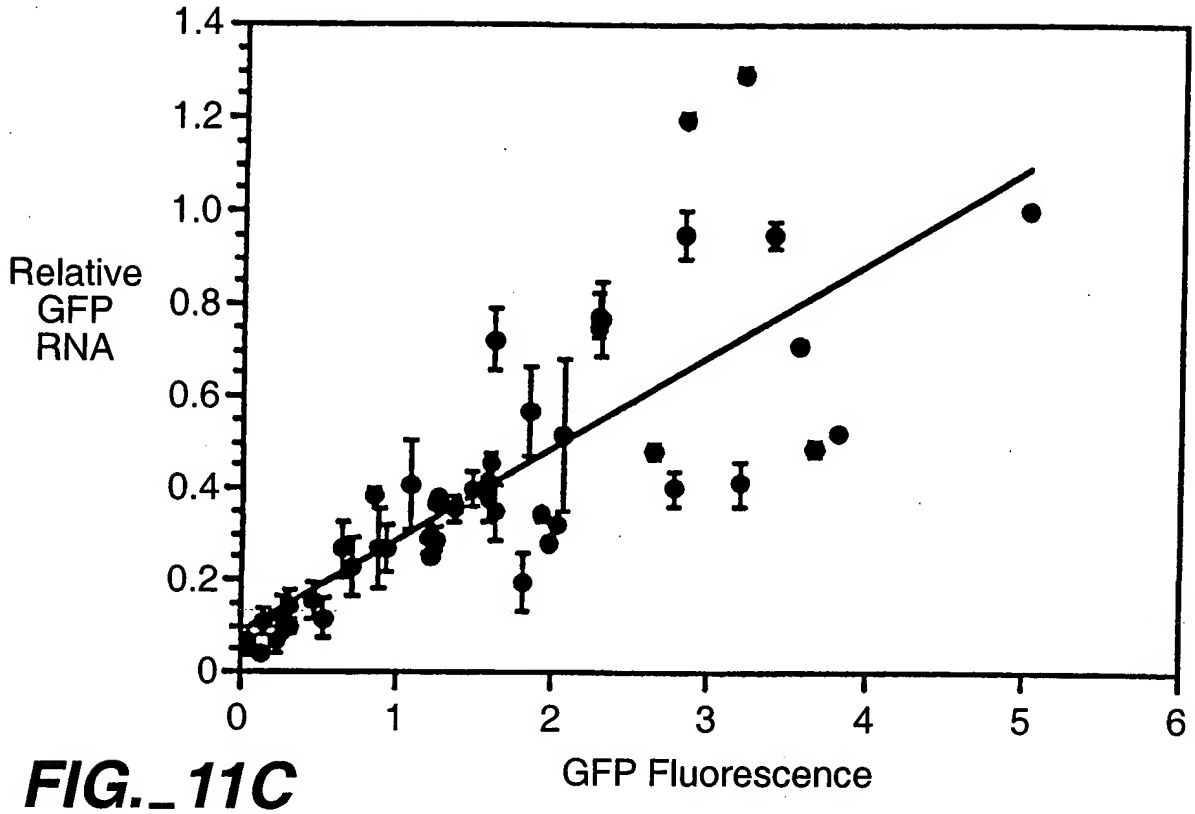


FIG._11C

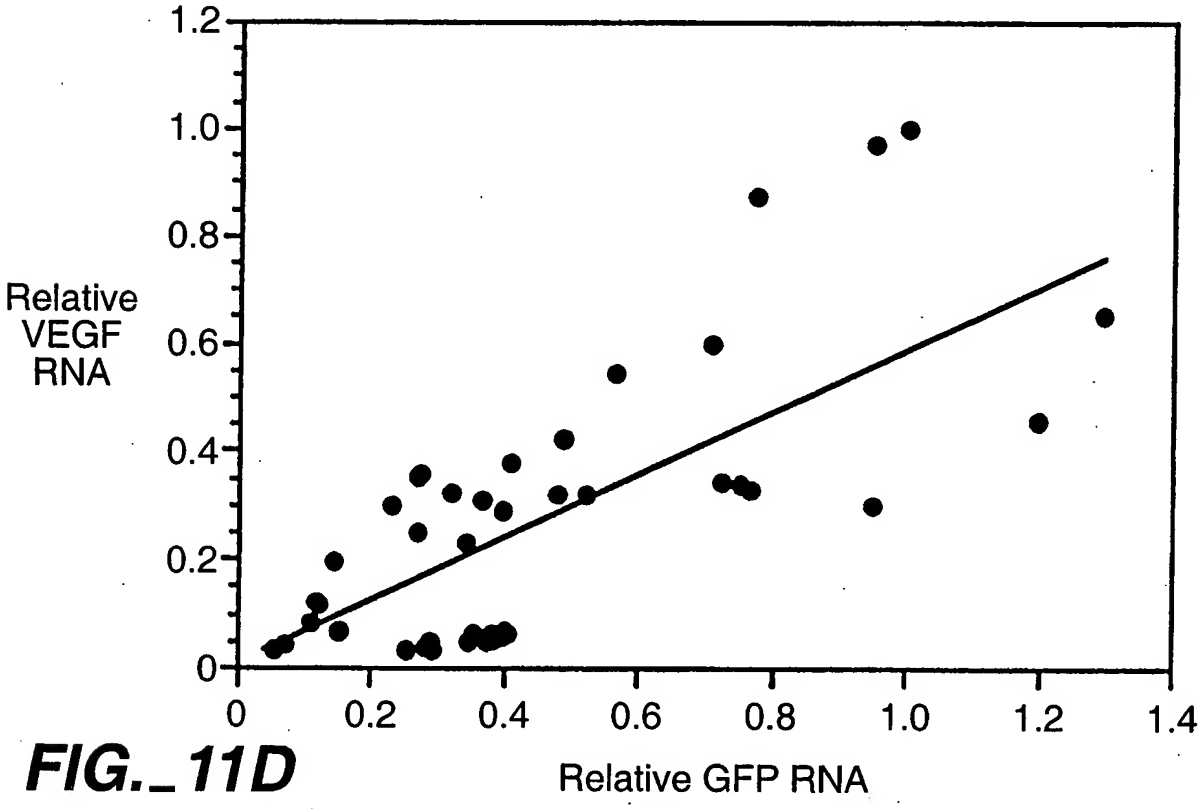


FIG._11D

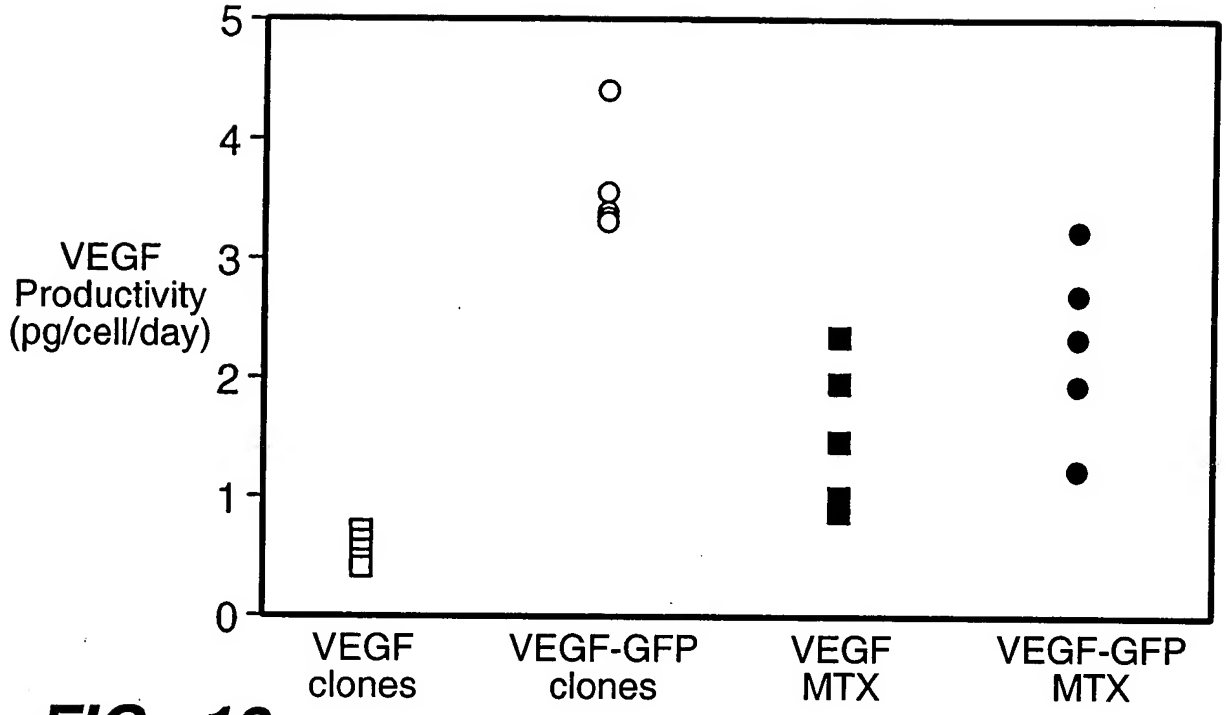

VEGF Productivity (pg/cell/day)
5
4
3
2
1
0
VEGF clones
VEGF-GFP clones
VEGF MTX
VEGF-GFP MTX

FIG._12

(E26) - LIGHT CHAIN

DIQLTQSPSS LSASVGDRVT ITCRASKPVD GEGDSYLNWY QQKPGKAPKL LIYAASYLES GVPSRFSGSG
SGTDFTLTIS SLQPEDFATY YCQQSHEDPY TFGQGTKVEI KRTVAAPSVF IFPPSDEQLK SGTASVVCLL
NNFYPREAKV QWKVDNALQS GNSQESVTEQ DSKDSTYSLS STLTLSKADY EKHKVYACEV THQGLSSPVT
KSFNRGEC

FIG._13A

(E26) - HEAVY CHAIN

EVQLVESGGG LVQPGGSLRL SCAVSGYSIT SGYSWNWIRQ APGKGLEWVA SITYDGSTNY NPSVKGRITI
SRDDSKNTFY LQMNSLRAED TAVYYCARGS HYFGHWHFAV WGQGTLVTVS SASTKGPSVF PLAPSSKSTS
GGTAALGCLV KDYFPEPVTV SWNSGALTSG VHTFPAVLQS SGLYSLSSVV TVPSSSLGTQ TYICNVNHKP
SNTKVDKKVE PKSCDKTHTC PPCPAPELLG GPSVFLFPPK PKDTLMISRT PEVTCVVVDV SHEDPEVKFN
WYVDGVEVHN AKTKPREEQY NSTYRVVSVL TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP
QVYTLPPSRE EMTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTTPP VLDSDGSFFL YSKLTVDKSR
WQQGNVFSCS VMHEALHNHY TQKSLSLSPG K

FIG._13B

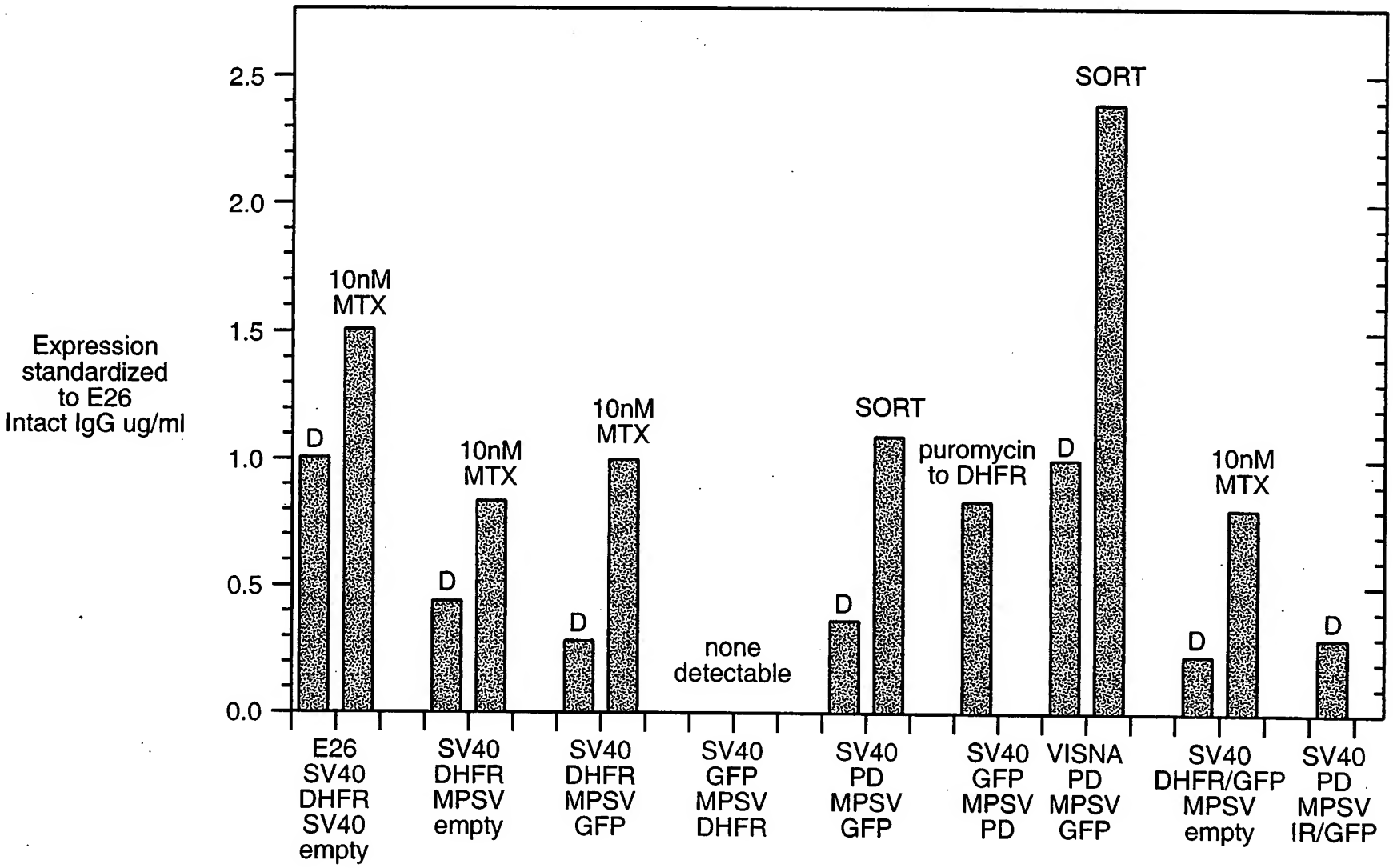

Expression standardized to E26 Intact IgG ug/ml
2.5
2.0
1.5
1.0
0.5
0.0
D
10nM MTX
10nM MTX
D
10nM MTX
D
none detectable
D
SORT
puromycin to DHFR
D
SORT
10nM MTX
D
D
E26 SV40 DHFR SV40 empty
SV40 DHFR MPSV empty
SV40 DHFR MPSV GFP
SV40 GFP MPSV DHFR
SV40 PD MPSV GFP
SV40 GFP MPSV PD
VISNA PD MPSV GFP
SV40 DHFR/GFP MPSV empty
SV40 PD MPSV IR/GFP

FIG._14

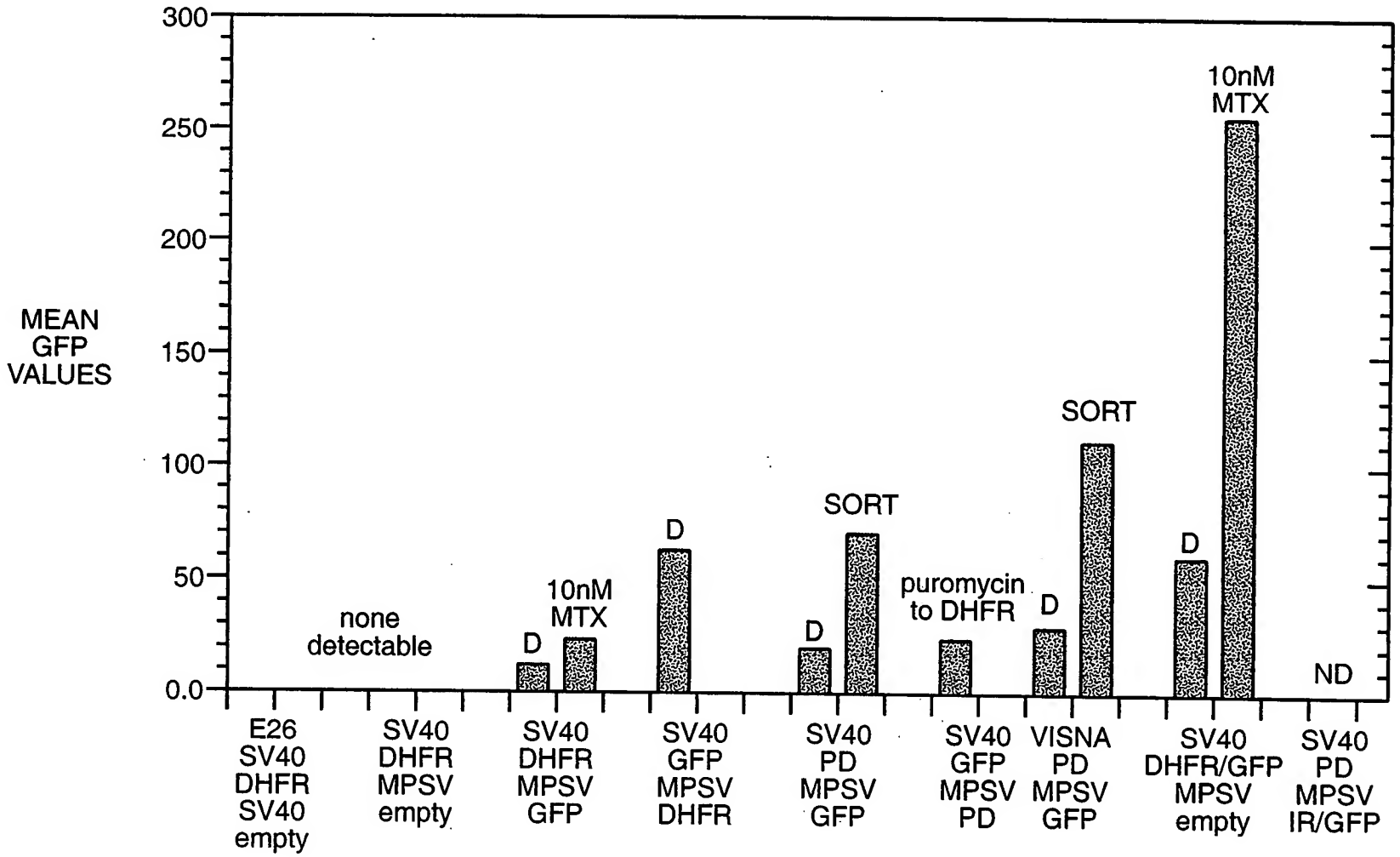

MEAN
GFP
VALUES
300
250
200
150
100
50
0.0
none
detectable
D
10nM
MTX
D
SORT
D
puromycin
to DHFR
D
SORT
D
10nM
MTX
ND
E26
SV40
DHFR
SV40
empty
SV40
DHFR
MPSV
empty
SV40
DHFR
MPSV
GFP
SV40
GFP
MPSV
DHFR
SV40
PD
MPSV
GFP
SV40
GFP
MPSV
PD
VISNA
PD
MPSV
GFP
SV40
DHFR/GFP
MPSV
empty
SV40
PD
MPSV
IR/GFP

FIG._15

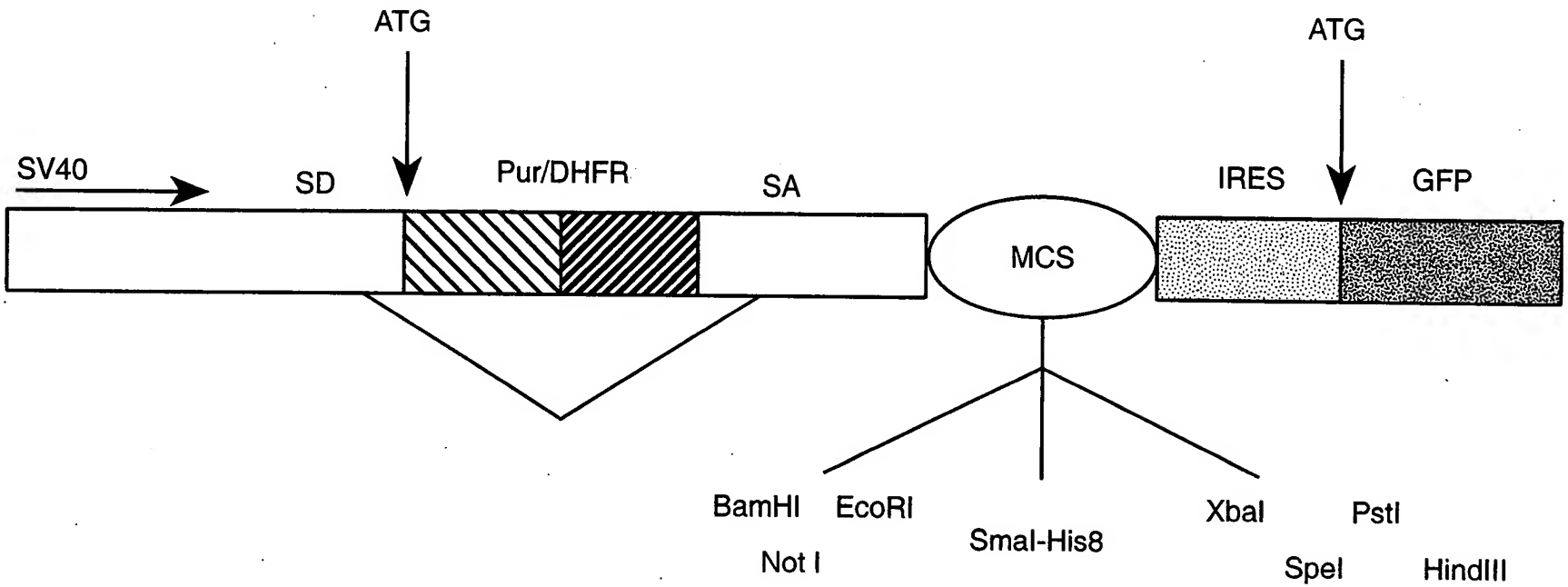
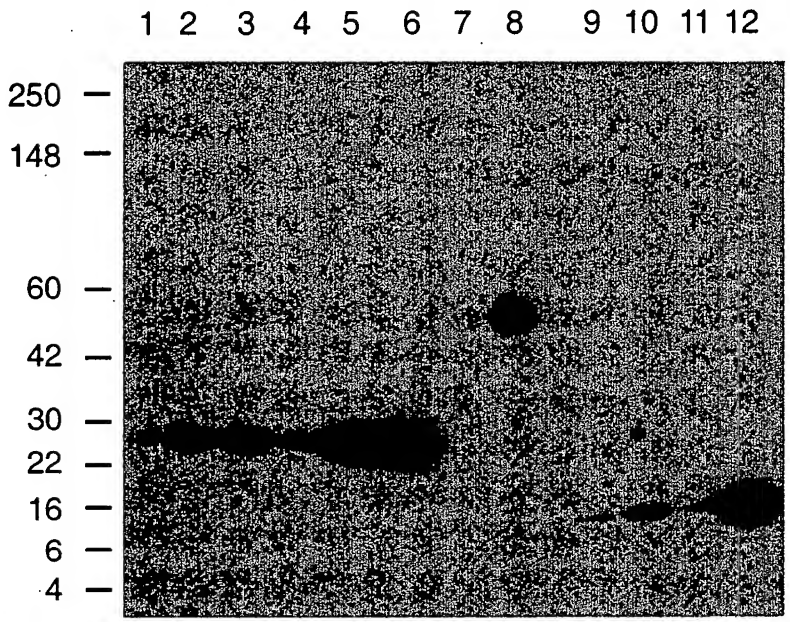

ATG
ATG
SV40
SD
Pur/DHFR
SA
IRES
GFP
MCS
BamHI
EcoRI
Not I
SmaI-His8
XbaI
PstI
SpeI
HindIII

FIG._16



Lane	DNA	Vector	Selection	Intensity
1	52196His	Standard	DHFR	1.0X
2	↓	↓	50nM MTX	3.5X
3	↓	IRES.GFP	Pur	3.7X
4	↓	↓	DHFR	2.4X
5	↓	↓	Medium sort	6.4X
6	↓	↓	High sort	7.3X
7	DP12	Negative		
8	Veg His	Standard	DHFR	N.A.
9	33222His	↓	DHFR	1.0X
10	↓	IRES.GFP	Pur	3.6X
11	↓	↓	DHFR	2.0X
12	↓	↓	High sort	12.7X

FIG._17

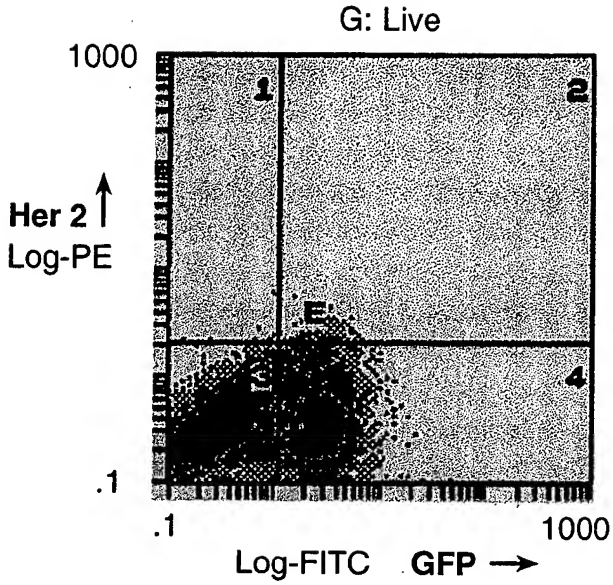


FIG._18A

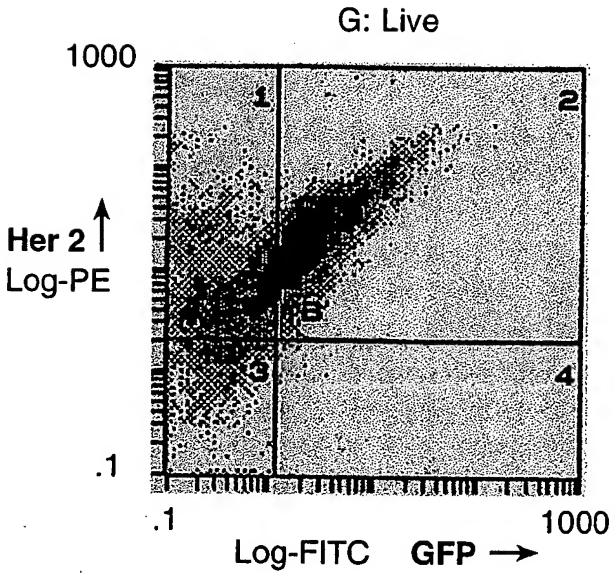


FIG._18B

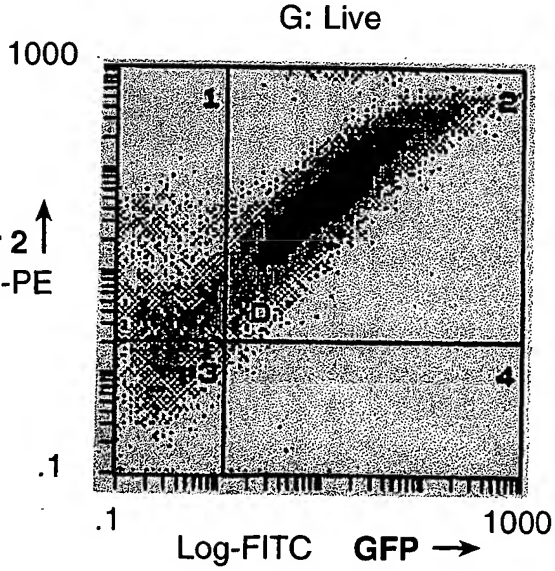


FIG._18C

VECTOR CONTROL

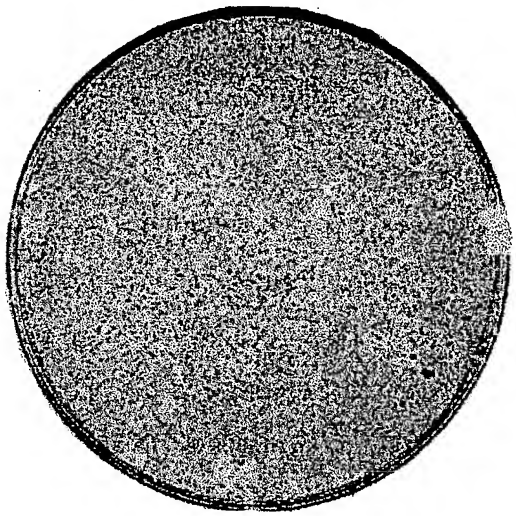


FIG._19A

HER 2 POOL

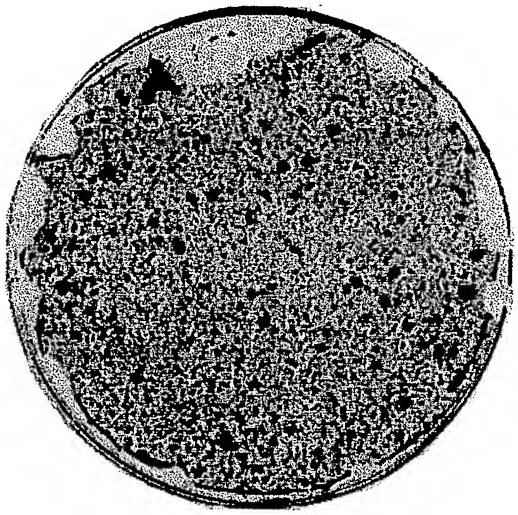


FIG._19B

HER 2 HIGH SORT

FIG._19C

Figure 20A. Plasmid SV40.IPD.Heterologous polypeptides

6 <400>

60 TTCGAGCTCG CCCGACATTG ATTATTGACT AGAGTCGATC GACAGCTGTG GAATGTGTGT

120 CAGTTAGGGT GTGGAAAGTC CCCAGGCTCC CCAGCAGGCA GAAGTATGCA AAGCATGCAT

180 CTCAATTAGT CAGCAACCAG GTGTGGAAAG TCCCCAGGCT CCCCAGCAGG CAGAAGTATG

240 CAAAGCATGC ATCTCAATTA GTCAGCAACC ATAGTCCCGC CCCTAACTCC GCCCATCCCG

300 CCCCTAACTC CGCCCAGTTC CGCCCATTCT CCGCCCCATG GCTGACTAAT TTTTTTTATT

360 TATGCAGAGG CCGAGGCCGC CTCGGCCTCT GAGCTATTCC AGAAGTAGTG AGGAGGCTTT

420 TTTGGAGGCC TAGGCTTTTG CAAAAAGCTA GCTTATCCGG CCGGGAACGG TGCATTGGAA

480 CGCGGATTCC CCGTGCCAAG AGTGACGTAA GTACCGCCTA TAGAGCGACT AGTCCACCAT

540 GACCGAGTAC AAGCCCACGG TGCGCCTCGC CACCCGCGAC GACGTCCCGC GGGCCGTACG

600 CACCCTCGCC GCCGCGTTCG CCGACTACCC CGCCACGCGC CACACCGTAG ACCCGGACCG

660 CCACATCGAG CGGGTCACCG AGCTGCAAGA ACTCTTCCTC ACGCGCGTCG GGCTCGACAT

720 CGGCAAGGTG TGGGTCGCGG ACGACGGCGC CGCGGTGGCG GTCTGGACCA CGCCGGAGAG

780 CGTCGAAGCG GGGGCGGTGT TCGCCGAGAT CGGCCCGCGC ATGGCCGAGT TGAGCGGTTC

840 CCGGCTGGCC GCGCAGCAAC AGATGGAAGG CCTCCTGGCG CCGCACCGGC CCAAGGAGCC

900 CGCGTGGTTC CTGGCCACCG TCGGCGTCTC GCCCGACCAC CAGGGCAAGG GTCTGGGCAG

960 CGCCGTCGTG CTCCCCGGAG TGGAGGCGGC CGAGCGCGCC GGGGTGCCCG CCTTCCTGGA

1020 GACCTCCGCG CCCCGCAACC TCCCCTTCTA CGAGCGGCTC GGCTTCACCG TCACCGCCGA

1080 CGTCGAGTGC CCGAAGGACC GCGCGACCTG GTGCATGACC CGCAAGCCCG GTGCCAACAT

1140 GGTTCGACCA TTGAACTGCA TCGTCGCCGT GTCCCAAAAT ATGGGGATTG GCAAGAACGG

1200 AGACCTACCC TGCCCTCCGC TCAGGAACGC GTTCAAGTAC TTCCAAAGAA TGACCACAAC

1260 CTCTTCAGTG GAAGGTAAAC AGAATCTGGT GATTATGGGT AGGAAAACCT GGTTCTCCAT

1320 TCCTGAGAAG AATCGACCTT TAAAGGACAG AATTAATATA GTTCTCAGTA GAGAACTCAA

1380 AGAACCACCA CGAGGAGCTC ATTTTCTTGC CAAAAGTTTG GATGATGCCT TAAGACTTAT

1440 TGAACAACCG GAATTGGCAA GTAAAGTAGA CATGGTTTGG ATAGTCGGAG GCAGTTCTGT

Figure 20B

1500 TTACCAGGAA GCCATGAATC AACCAGGCCA CCTTAGACTC TTTGTGACAA GGATCATGCA

1560 GGAATTTGAA AGTGACACGT TTTTCCCAGA AATTGATTTG GGGAAATATA AACCTCTCCC

1620 AGAATACCCA GGCGTCCTCT CTGAGGTCCA GGAGGAAAAA GGCATCAAGT ATAAGTTTGA

1680 AGTCTACGAG AAGAAAGACT AACGTTAACT GCTCCCCTCC TAAAGCTATG CATTTTTATA

1740 AGACCATGGG ACTTTTGCTG GCTTTAGATC CCCTTGGCTT CGTTAGAACG CAGCTACAAT

1800 TAATACATAA CCTTATGTAT CATACACATA CGATTTAGGT GACACTATAG ATAACATCCA

1860 CTTTGCCTTT CTCTCCACAG GTGTCCACTC CCAGGTCCAA CTGCACCTCG GTTCTATCGA

1920 TTGAATTCCA CC <from 1921 to 3381, insertion site for a selected heterologous polypeptide>

3382 CGATGGCC GCCATGGCCC AACTTGTTTA TTGCAGCTTA

3420 TAATGGTTAC AAATAAAGCA ATAGCATCAC AAATTTCACA AATAAAGCAT TTTTTTCACT

3480 GCATTCTAGT TGTGGTTTGT CCAAACTCAT CAATGTATCT TATCATGTCT GGATCGGGAA

3540 TTAATTCGGC GCAGCACCAT GGCCTGAAAT AACCTCTGAA AGAGGAACTT GGTTAGGTAC

3600 CTTCTGAGGC GGAAAGAACC AGCTGTGGAA TGTGTGTCAG TTAGGGTGTG GAAAGTCCCC

3660 AGGCTCCCCA GCAGGCAGAA GTATGCAAAG CATGCATCTC AATTAGTCAG CAACCAGGTG

3720 TGGAAAGTCC CCAGGCTCCC CAGCAGGCAG AAGTATGCAA AGCATGCATC TCAATTAGTC

3780 AGCAACCATA GTCCCGCCCC TAACTCCGCC CATCCCGCCC CTAACTCCGC CCAGTTCCGC

3840 CCATTCTCCG CCCCATGGCT GACTAATTTT TTTTATTTAT GCAGAGGCCG AGGCCGCCTC

3900 GGCCTCTGAG CTATTCCAGA AGTAGTGAGG AGGCTTTTTT GGAGGAGCTT TTGCAAAAAG

3960 CTAGCTTATC CGGCCGGGAA CGGTGCATTG GAACGCGGAT TCCCCGTGCC AAGAGTCAGG

4020 TAAGTACCGC CTATAGAGTC TATAGGCCCA CCCCCTTGGC TTCGTTAGAA CGCGGCTACA

4080 ATTAATACAT AACCTTTTGG ATCGATCCTA CTGACACTGA CATCCACTTT TTCTTTTTCT

4140 CCACAGGTGT CCACTCCCAG GTCCAACTGC ACCTCGGTTC GCGAAGCTAG CTTGGGCTGC

4200 ATCGATTGAA TTCCACC <from 4217 to 4919, insertion site for a selected heterologous polypeptide>

Figure 20C

4920 CGATGGCCGC CATGGCCCAA CTTGTTTATT GCAGCTTATA ATGGTTACAA ATAAAGCAAT

4980 AGCATCACAA ATTTCACAAA TAAAGCATTT TTTTCACTGC ATTCTAGTTG TGGTTTGTCC

5040 AAACTCATCA ATGTATCTTA TCATGTCTGG ATCGGGAATT AATTCGGCGC AGCACCATGG

5100 CCTGAAATAA GTTTAAACCC TCTGAAAGAG GAACTTGGTT AGGTACCGAC TAGTCTTTTG

5160 CAAAAAGCTG TTACCTCGAG CGGCCGCTTA ATTAAGGCGC GCCATTTAAA TCCTGCAGGT

5220 AACAGCTTGG CACTGGCCGT CGTTTTACAA CGTCGTGACT GGGAAAACCC TGGCGTTACC

5280 CAACTTAATC GCCTTGCAGC ACATCCCCCT TTCGCCAGCT GGCGTAATAG CGAAGAGGCC

5340 CGCACCGATC GCCCTTCCCA ACAGTTGCGC AGCCTGAATG GCGAATGGCG CCTGATGCGG

5400 TATTTTCTCC TTACGCATCT GTGCGGTATT TCACACCGCA TACGTCAAAG CAACCATAGT

5460 ACGCGCCCTG TAGCGGCGCA TTAAGCGCGG CGGGTGTGGT GGTTACGCGC AGCGTGACCG

5520 CTACACTTGC CAGCGCCCTA GCGCCCGCTC CTTTCGCTTT CTTCCCTTCC TTTCTCGCCA

5580 CGTTCGCCGG CTTTCCCCGT CAAGCTCTAA ATCGGGGGCT CCCTTTAGGG TTCCGATTTA

5640 GTGCTTTACG GCACCTCGAC CCCAAAAAAC TTGATTTGGG TGATGGTTCA CGTAGTGGGC

5700 CATCGCCCTG ATAGACGGTT TTTCGCCCTT TGACGTTGGA GTCCACGTTC TTTAATAGTG

5760 GACTCTTGTT CCAAACTGGA ACAACACTCA ACCCTATCTC GGGCTATTCT TTTGATTTAT

5820 AAGGGATTTT GCCGATTTCG GCCTATTGGT TAAAAAATGA GCTGATTTAA CAAAAATTTA

5880 ACGCGAATTT TAACAAAATA TTAACGTTTA CAATTTTATG GTGCACTCTC AGTACAATCT

5940 GCTCTGATGC CGCATAGTTA AGCCAGCCCC GACACCCGCC AACACCCGCT GACGCGCCCT

6000 GACGGGCTTG TCTGCTCCCG GCATCCGCTT ACAGACAAGC TGTGACCGTC TCCGGGAGCT

6060 GCATGTGTCA GAGGTTTTCA CCGTCATCAC CGAAACGCGC GACGAAAGGG CCTCGTGATA

6120 CGCCTATTTT TATAGGTTAA TGTCATGATA ATAATGGTTT CTTAGACGTC AGGTGGCACT

6180 TTTCGGGGAA ATGTGCGCGG AACCCCTATT TGTTTATTTT TCTAAATACA TTCAAATATG

6240 TATCCGCTCA TGAGACAATA ACCCTGATAA ATGCTTCAAT AATATTGAAA AAGGAAGAGT

6300 ATGAGTATTC AACATTTCCG TGTCGCCCTT ATTCCCTTTT TTGCGGCATT TTGCCTTCCT

6360 GTTTTTGCTC ACCCAGAAAC GCTGGTGAAA GTAAAAGATG CTGAAGATCA GTTGGGTGCA

Figure 20D

6420 CGAGTGGGTT ACATCGAACT GGATCTCAAC AGCGGTAAGA TCCTTGAGAG TTTTCGCCCC

6480 GAAGAACGTT TTCCAATGAT GAGCACTTTT AAAGTTCTGC TATGTGGCGC GGTATTATCC

6540 CGTATTGACG CCGGGCAAGA GCAACTCGGT CGCCGCATAC ACTATTCTCA GAATGACTTG

6600 GTTGAGTACT CACCAGTCAC AGAAAAGCAT CTTACGGATG GCATGACAGT AAGAGAATTA

6660 TGCAGTGCTG CCATAACCAT GAGTGATAAC ACTGCGGCCA ACTTACTTCT GACAACGATC

6720 GGAGGACCGA AGGAGCTAAC CGCTTTTTTG CACAACATGG GGGATCATGT AACTCGCCTT

6780 GATCGTTGGG AACCGGAGCT GAATGAAGCC ATACCAAACG ACGAGCGTGA CACCACGATG

6840 CCTGTAGCAA TGGCAACAAC GTTGCGCAAA CTATTAACTG GCGAACTACT TACTCTAGCT

6900 TCCCGGCAAC AATTAATAGA CTGGATGGAG GCGGATAAAG TTGCAGGACC ACTTCTGCGC

6960 TCGGCCCTTC CGGCTGGCTG GTTTATTGCT GATAAATCTG GAGCCGGTGA GCGTGGGTCT

7020 CGCGGTATCA TTGCAGCACT GGGGCCAGAT GGTAAGCCCT CCCGTATCGT AGTTATCTAC

7080 ACGACGGGGA GTCAGGCAAC TATGGATGAA CGAAATAGAC AGATCGCTGA GATAGGTGCC

7140 TCACTGATTA AGCATTGGTA ACTGTCAGAC CAAGTTTACT CATATATACT TTAGATTGAT

7200 TTAAAACTTC ATTTTTAATT TAAAAGGATC TAGGTGAAGA TCCTTTTTGA TAATCTCATG

7260 ACCAAAATCC CTTAACGTGA GTTTTCGTTC CACTGAGCGT CAGACCCCGT AGAAAAGATC

7320 AAAGGATCTT CTTGAGATCC TTTTTTTCTG CGCGTAATCT GCTGCTTGCA AACAAAAAAA

7380 CCACCGCTAC CAGCGGTGGT TTGTTTGCCG GATCAAGAGC TACCAACTCT TTTTCCGAAG

7440 GTAACTGGCT TCAGCAGAGC GCAGATACCA AATACTGTCC TTCTAGTGTA GCCGTAGTTA

7500 GGCCACCACT TCAAGAACTC TGTAGCACCG CCTACATACC TCGCTCTGCT AATCCTGTTA

7560 CCAGTGGCTG CTGCCAGTGG CGATAAGTCG TGTCTTACCG GGTTGGACTC AAGACGATAG

7620 TTACCGGATA AGGCGCAGCG GTCGGGCTGA ACGGGGGGTT CGTGCACACA GCCCAGCTTG

7680 GAGCGAACGA CCTACACCGA ACTGAGATAC CTACAGCGTG AGCTATGAGA AAGCGCCACG

7740 CTTCCCGAAG GGAGAAAGGC GGACAGGTAT CCGGTAAGCG GCAGGGTCGG AACAGGAGAG

7800 CGCACGAGGG AGCTTCCAGG GGGAAACGCC TGGTATCTTT ATAGTCCTGT CGGGTTTCGC

7860 CACCTCTGAC TTGAGCGTCG ATTTTTGTGA TGCTCGTCAG GGGGGCGGAG CCTATGGAAA

Figure 20E

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7920  AACGCCAGCA ACGCGGCCTT TTTACGGTTC CTGGCCTTTT GCTGGCCTTT TGCTCACATG
7980  TTCTTTCCTG CGTTATCCCC TGATTCTGTG GATAACCGTA TTACCGCCTT TGAGTGAGCT
8040  GATACCGCTC GCCGCAGCCG AACGACCGAG CGCAGCGAGT CAGTGAGCGA GGAAGCGGAA
8100  GAGCGCCCAA TACGCAAACC GCCTCTCCCC GCGCGTTGGC CGATTCATTA ATGCAGCTGG
8160  CACGACAGGT TTCCCGACTG GAAAGCGGGC AGTGAGCGCA ACGCAATTAA TGTGAGTTAG
8220  CTCACTCATT AGGCACCCCA GGCTTTACAC TTTATGCTTC CGGCTCGTAT GTTGTGTGGA
8277  ATTGTGAGCG GATAACAATT TCACACAGGA AACAGCTATG ACATGATTAC GAATTAA
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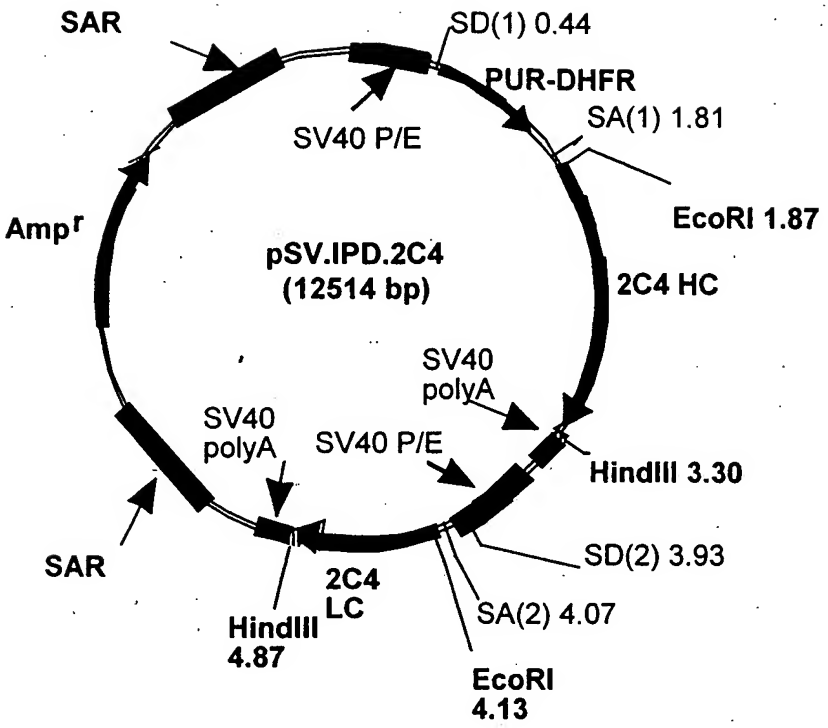
SAR
SD(1) 0.44
PUR-DHFR
SA(1) 1.81
SV40 P/E
EcoRI 1.87
Amp^r
pSV.IPD.2C4
(12514 bp)
2C4 HC
SV40
polyA
SV40
polyA
SV40 P/E
HindIII 3.30
SD(2) 3.93
SAR
2C4
LC
SA(2) 4.07
HindIII
4.87
EcoRI
4.13

Figure 21

Figure 22A

pSV.IPD.2C4

length: 12514 (circular)

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   1 TTCGAGCTCG CCCGACATTG ATTATTGACT AGAGTCGATC GACAGCTGTG GAATGTGTGT CAGTTAGGGT GTGGAAAGTC CCCAGGCTCC CCAGCAGGCA
     AAGCTCGAGC GGGCTGTAAC TAATAACTGA TCTCAGCTAG CTGTCGACAC CTTACACACA GTCAATCCCA CACCTTTCAG GGGTCCGAGG GGTCGTCCGT

 101 GAAGTATGCA AAGCATGCAT CTCAATTAGT CAGCAACCAG GTGTGGAAAG TCCCCAGGCT CCCCAGCAGG CAGAAGTATG CAAAGCATGC ATCTCAATTA
     CTTCATACGT TTCGTACGTA GAGTTAATCA GTCGTTGGTC CACACCTTTC AGGGGTCCGA GGGGTCGTCC GTCTTCATAC GTTTCGTACG TAGAGTTAAT

 201 GTCAGCAACC ATAGTCCCGC CCCTAACTCC GCCCATCCCG CCCCTAACTC CGCCCAGTTC CGCCCATTCT CCGCCCCATG GCTGACTAAT TTTTTTTATT
     CAGTCGTTGG TATCAGGGCG GGGATTGAGG CGGGTAGGGC GGGGATTGAG GCGGGTCAAG GCGGGTAAGA GGCGGGGTAC CGACTGATTA AAAAAAATAA

 301 TATGCAGAGG CCGAGGCCGC CTCGGCCTCT GAGCTATTCC AGAAGTAGTG AGGAGGCTTT TTTGGAGGCC TAGGCTTTTG CAAAAAGCTA GCTTATCCGG
     ATACGTCTCC GGCTCCGGCG GAGCCGGAGA CTCGATAAGG TCTTCATCAC TCCTCCGAAA AAACCTCCGG ATCCGAAAAC GTTTTTCGAT CGAATAGGCC

 401 CCGGGAACGG TGCATTGGAA CGCGGATTCC CCGTGCCAAG AGTGACGTAA GTACCGCCTA TAGAGCGACT AGTCCACCAT GACCGAGTAC AAGCCCACGG
     GGCCCTTGCC ACGTAACCTT GCGCCTAAGG GGCACGGTTC TCACTGCATT CATGGCGGAT ATCTCGCTGA TCAGGTGGTA CTGGCTCATG TTCGGGTGCC
                                                ^splice donor                          ^Start PUR coding
 501 TGCGCCTCGC CACCCGCGAC GACGTCCCGC GGGCCGTACG CACCCTCGCC GCCGCGTTCG CCGACTACCC CGCCACGCGC CACACCGTAG ACCCGGACCG
     ACGCGGAGCG GTGGGCGCTG CTGCAGGGCG CCCGGCATGC GTGGGAGCGG CGGCGCAAGC GGCTGATGGG GCGGTGCGCG GTGTGGCATC TGGGCCTGGC

 601 CCACATCGAG CGGGTCACCG AGCTGCAAGA ACTCTTCCTC ACGCGCGTCG GGCTCGACAT CGGCAAGGTG TGGGTCGCGG ACGACGGCGC CGCGGTGGCG
     GGTGTAGCTC GCCCAGTGGC TCGACGTTCT TGAGAAGGAG TGCGCGCAGC CCGAGCTGTA GCCGTTCCAC ACCCAGCGCC TGCTGCCGCG GCGCCACCGC

 701 GTCTGGACCA CGCCGGAGAG CGTCGAAGCG GGGGCGGTGT TCGCCGAGAT CGGCCCGCGC ATGGCCGAGT TGAGCGGTTC CCGGCTGGCC GCGCAGCAAC
     CAGACCTGGT GCGGCCTCTC GCAGCTTCGC CCCCGCCACA AGCGGCTCTA GCCGGGCGCG TACCGGCTCA ACTCGCCAAG GGCCGACCGG CGCGTCGTTG

 801 AGATGGAAGG CCTCCTGGCG CCGCACCGGC CCAAGGAGCC CGCGTGGTTC CTGGCCACCG TCGGCGTCTC GCCCGACCAC CAGGGCAAGG GTCTGGGCAG
     TCTACCTTCC GGAGGACCGC GGCGTGGCCG GGTTCCTCGG GCGCACCAAG GACCGGTGGC AGCCGCAGAG CGGGCTGGTG GTCCCGTTCC CAGACCCGTC

 901 CGCCGTCGTG CTCCCCGGAG TGGAGGCGGC CGAGCGCGCC GGGGTGCCCG CCTTCCTGGA GACCTCCGCG CCCCGCAACC TCCCCTTCTA CGAGCGGCTC
     GCGGCAGCAC GAGGGGCCTC ACCTCCGCCG GCTCGCGCGG CCCCACGGGC GGAAGGACCT CTGGAGGCGC GGGGCGTTGG AGGGGAAGAT GCTCGCCGAG

1001 GGCTTCACCG TCACCGCCGA CGTCGAGTGC CCGAAGGACC GCGCGACCTG GTGCATGACC CGCAAGCCCG GTGCCAACAT GGTTCGACCA TTGAACTGCA
     CCGAAGTGGC AGTGGCGGCT GCAGCTCACG GGCTTCCTGG CGCGCTGGAC CACGTACTGG GCGTTCGGGC CACGGTTGTA CCAAGCTGGT AACTTGACGT
                                                                                    ^Start DHFR coding
1101 TCGTCGCCGT GTCCCAAAAT ATGGGGATTG GCAAGAACGG AGACCTACCC TGCCCTCCGC TCAGGAACGC GTTCAAGTAC TTCCAAAGAA TGACCACAAC
     AGCAGCGGCA CAGGGTTTTA TACCCCTAAC CGTTCTTGCC TCTGGATGGG ACGGGAGGCG AGTCCTTGCG CAAGTTCATG AAGGTTTCTT ACTGGTGTTG

1201 CTCTTCAGTG GAAGGTAAAC AGAATCTGGT GATTATGGGT AGGAAAACCT GGTTCTCCAT TCCTGAGAAG AATCGACCTT TAAAGGACAG AATTAATATA
     GAGAAGTCAC CTTCCATTTG TCTTAGACCA CTAATACCCA TCCTTTTGGA CCAAGAGGTA AGGACTCTTC TTAGCTGGAA ATTTCCTGTC TTAATTATAT

1301 GTTCTCAGTA GAGAACTCAA AGAACCACCA CGAGGAGCTC ATTTTCTTGC CAAAAGTTTG GATGATGCCT TAAGACTTAT TGAACAACCG GAATTGGCAA
     CAAGAGTCAT CTCTTGAGTT TCTTGGTGGT GCTCCTCGAG TAAAAGAACG GTTTTCAAAC CTACTACGGA ATTCTGAATA ACTTGTTGGC CTTAACCGTT

1401 GTAAAGTAGA CATGGTTTGG ATAGTCGGAG GCAGTTCTGT TTACCAGGAA GCCATGAATC AACCAGGCCA CCTTAGACTC TTTGTGACAA GGATCATGCA
     CATTTCATCT GTACCAAACC TATCAGCCTC CGTCAAGACA AATGGTCCTT CGGTACTTAG TTGGTCCGGT GGAATCTGAG AAACACTGTT CCTAGTACGT

1501 GGAATTTGAA AGTGACACGT TTTTCCCAGA AATTGATTTG GGGAAATATA AACCTCTCCC AGAATACCCA GGCGTCCTCT CTGAGGTCCA GGAGGAAAAA
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     CCTTAAACTT TCACTGTGCA AAAAGGGTCT TTAACTAAAC CCCTTTATAT TTGGAGAGGG TCTTATGGGT CCGCAGGAGA GACTCCAGGT CCTCCTTTTT

1601 GGCATCAAGT ATAAGTTTGA AGTCTACGAG AAGAAAGACT AACGTTAACT GCTCCCCTCC TAAAGCTATG CATTTTTATA AGACCATGGG ACTTTTGCTG
     CCGTAGTTCA TATTCAAACT TCAGATGCTC TTCTTTCTGA TTGCAATTGA CGAGGGGAGG ATTTCGATAC GTAAAAATAT TCTGGTACCC TGAAAACGAC
                                                ^End DHFR
1701 GCTTTAGATC CCCTTGGCTT CGTTAGAACG CAGCTACAAT TAATACATAA CCTTATGTAT CATACACATA CGATTTAGGT GACACTATAG AATAACATCC
     CGAAATCTAG GGGAACCGAA GCAATCTTGC GTCGATGTTA ATTATGTATT GGAATACATA GTATGTGTAT GCTAAATCCA CTGTGATATC TTATTGTAGG

1801 ACTTTGCCTT TCTCTCCACA GGTGTCCACT CCCAGGTCCA ACTGCACCTC GGTTCTATCG ATTGAATTCC ACCATGGGAT GGTCATGTAT CATCCTTTTT
     TGAAACGGAA AGAGAGGTGT CCACAGGTGA GGGTCCAGGT TGACGTGGAG CCAAGATAGC TAACTTAAGG TGGTACCCTA CCAGTACATA GTAGGAAAAA
                                                                                    ^Start 2C4 HCcoding
1901 CTAGTAGCAA CTGCAACTGG AGTACATTCA GAAGTTCAGC TGGTGGAGTC TGGCGGTGGC CTGGTGCAGC CAGGGGGCTC ACTCCGTTTG TCCTGTGCAG
     GATCATCGTT GACGTTGACC TCATGTAAGT CTTCAAGTCG ACCACCTCAG ACCGCCACCG GACCACGTCG GTCCCCCGAG TGAGGCAAAC AGGACACGTC

2001 CTTCTGGCTT CACCTTCACC GACTATACCA TGGACTGGGT CCGTCAGGCC CCGGGTAAGG GCCTGGAATG GGTTGCAGAT GTTAATCCTA ACAGTGGCGG
     GAAGACCGAA GTGGAAGTGG CTGATATGGT ACCTGACCCA GGCAGTCCGG GGCCCATTCC CGGACCTTAC CCAACGTCTA CAATTAGGAT TGTCACCGCC

2101 CTCTATCTAT AACCAGCGCT TCAAGGGCCG TTTCACTCTG AGTGTTGACA GATCTAAAAA CACATTATAC CTGCAGATGA ACAGCCTGCG TGCTGAGGAC
     GAGATAGATA TTGGTCGCGA AGTTCCCGGC AAAGTGAGAC TCACAACTGT CTAGATTTTT GTGTAATATG GACGTCTACT TGTCGGACGC ACGACTCCTG

2201 ACTGCCGTCT ATTATTGTGC TCGTAACCTG GGACCCTCTT TCTACTTTGA CTACTGGGGT CAAGGAACCC TGGTCACCGT CTCCTCGGCC TCCACCAAGG
     TGACGGCAGA TAATAACACG AGCATTGGAC CCTGGGAGAA AGATGAAACT GATGACCCCA GTTCCTTGGG ACCAGTGGCA GAGGAGCCGG AGGTGGTTCC

2301 GCCCATCGGT CTTCCCCCTG GCACCCTCCT CCAAGAGCAC CTCTGGGGGC ACAGCGGCCC TGGGCTGCCT GGTCAAGGAC TACTTCCCCG AACCGGTGAC
     CGGGTAGCCA GAAGGGGGAC CGTGGGAGGA GGTTCTCGTG GAGACCCCCG TGTCGCCGGG ACCCGACGGA CCAGTTCCTG ATGAAGGGGC TTGGCCACTG

2401 GGTGTCGTGG AACTCAGGCG CCCTGACCAG CGGCGTGCAC ACCTTCCCGG CTGTCCTACA GTCCTCAGGA CTCTACTCCC TCAGCAGCGT GGTGACTGTG
     CCACAGCACC TTGAGTCCGC GGGACTGGTC GCCGCACGTG TGGAAGGGCC GACAGGATGT CAGGAGTCCT GAGATGAGGG AGTCGTCGCA CCACTGACAC

2501 CCCTCTAGCA GCTTGGGCAC CCAGACCTAC ATCTGCAACG TGAATCACAA GCCCAGCAAC ACCAAGGTGG ACAAGAAAGT TGAGCCCAAA TCTTGTGACA
     GGGAGATCGT CGAACCCGTG GGTCTGGATG TAGACGTTGC ACTTAGTGTT CGGGTCGTTG TGGTTCCACC TGTTCTTTCA ACTCGGGTTT AGAACACTGT

2601 AAACTCACAC ATGCCCACCG TGCCCAGCAC CTGAACTCCT GGGGGGACCG TCAGTCTTCC TCTTCCCCCC AAAACCCAAG GACACCCTCA TGATCTCCCG
     TTTGAGTGTG TACGGGTGGC ACGGGTCGTG GACTTGAGGA CCCCCCTGGC AGTCAGAAGG AGAAGGGGGG TTTTGGGTTC CTGTGGGAGT ACTAGAGGGC

2701 GACCCCTGAG GTCACATGCG TGGTGGTGGA CGTGAGCCAC GAAGACCCTG AGGTCAAGTT CAACTGGTAC GTGGACGGCG TGGAGGTGCA TAATGCCAAG
     CTGGGGACTC CAGTGTACGC ACCACCACCT GCACTCGGTG CTTCTGGGAC TCCAGTTCAA GTTGACCATG CACCTGCCGC ACCTCCACGT ATTACGGTTC

2801 ACAAAGCCGC GGGAGGAGCA GTACAACAGC ACGTACCGGG TGGTCAGCGT CCTCACCGTC CTGCACCAGG ACTGGCTGAA TGGCAAGGAG TACAAGTGCA
     TGTTTCGGCG CCCTCCTCGT CATGTTGTCG TGCATGGCCC ACCAGTCGCA GGAGTGGCAG GACGTGGTCC TGACCGACTT ACCGTTCCTC ATGTTCACGT

2901 AGGTCTCCAA CAAAGCCCTC CCAGCCCCCA TCGAGAAAAC CATCTCCAAA GCCAAAGGGC AGCCCCGAGA ACCACAGGTG TACACCCTGC CCCCATCCCG
     TCCAGAGGTT GTTTCGGGAG GGTCGGGGGT AGCTCTTTTG GTAGAGGTTT CGGTTTCCCG TCGGGGCTCT TGGTGTCCAC ATGTGGGACG GGGGTAGGGC

3001 GGAAGAGATG ACCAAGAACC AGGTCAGCCT GACCTGCCTG GTCAAAGGCT TCTATCCCAG CGACATCGCC GTGGAGTGGG AGAGCAATGG GCAGCCGGAG
     CCTTCTCTAC TGGTTCTTGG TCCAGTCGGA CTGGACGGAC CAGTTTCCGA AGATAGGGTC GCTGTAGCGG CACCTCACCC TCTCGTTACC CGTCGGCCTC

3101 AACAACTACA AGACCACGCC TCCCGTGCTG GACTCCGACG GCTCCTTCTT CCTCTACAGC AAGCTCACCG TGGACAAGAG CAGGTGGCAG CAGGGGAACG
     TTGTTGATGT TCTGGTGCGG AGGGCACGAC CTGAGGCTGC CGAGGAAGAA GGAGATGTCG TTCGAGTGGC ACCTGTTCTC GTCCACCGTC GTCCCCTTGC

3201 TCTTCTCATG CTCCGTGATG CATGAGGCTC TGCACAACCA CTACACGCAG AAGAGCCTCT CCCTGTCTCC GGGTAAATGA GTGCGACGGC CCTAGAGTCG
     AGAAGAGTAC GAGGCACTAC GTACTCCGAG ACGTGTTGGT GATGTGCGTC TTCTCGGAGA GGGACAGAGG CCCATTTACT CACGCTGCCG GGATCTCAGC
```

Figure 22B

```
3301 ACCTGCAGAA GCTTCGATGG CCGCCATGGC CCAACTTGTT TATTGCAGCT TATAATGGTT ACAAATAAAG CAATAGCATC ACAAATTTCA CAAATAAAGC
     TGGACGTCTT CGAAGCTACC GGCGGTACCG GGTTGAACAA ATAACGTCGA ATATTACCAA TGTTTATTTC GTTATCGTAG TGTTTAAAGT GTTTATTTCG

3401 ATTTTTTTCA CTGCATTCTA GTTGTGGTTT GTCCAAACTC ATCAATGTAT CTTATCATGT CTGGATCGGG AATTAATTCG GCGCAGCACC ATGGCCTGAA
     TAAAAAAAGT GACGTAAGAT CAACACCAAA CAGGTTTGAG TAGTTACATA GAATAGTACA GACCTAGCCC TTAATTAAGC CGCGTCGTGG TACCGGACTT

3501 ATAACCTCTG AAAGAGGAAC TTGGTTAGGT ACCTTCTGAG GCGGAAAGAA CCAGCTGTGG AATGTGTGTC AGTTAGGGTG TGGAAAGTCC CCAGGCTCCC
     TATTGGAGAC TTTCTCCTTG AACCAATCCA TGGAAGACTC CGCCTTTCTT GGTCGACACC TTACACACAG TCAATCCCAC ACCTTTCAGG GGTCCGAGGG

3601 CAGCAGGCAG AAGTATGCAA AGCATGCATC TCAATTAGTC AGCAACCAGG TGTGGAAAGT CCCCAGGCTC CCCAGCAGGC AGAAGTATGC AAAGCATGCA
     GTCGTCCGTC TTCATACGTT TCGTACGTAG AGTTAATCAG TCGTTGGTCC ACACCTTTCA GGGGTCCGAG GGGTCGTCCG TCTTCATACG TTTCGTACGT

3701 TCTCAATTAG TCAGCAACCA TAGTCCCGCC CCTAACTCCG CCCATCCCGC CCCTAACTCC GCCCAGTTCC GCCCATTCTC CGCCCCATGG CTGACTAATT
     AGAGTTAATC AGTCGTTGGT ATCAGGGCGG GGATTGAGGC GGGTAGGGCG GGGATTGAGG CGGGTCAAGG CGGGTAAGAG GCGGGGTACC GACTGATTAA

3801 TTTTTTATTT ATGCAGAGGC CGAGGCCGCC TCGGCCTCTG AGCTATTCCA GAAGTAGTGA GGAGGCTTTT TTGGAGGACT AGGCTTTTGC AAAAAGCTAG
     AAAAAATAAA TACGTCTCCG GCTCCGGCGG AGCCGGAGAC TCGATAAGGT CTTCATCACT CCTCCGAAAA AACCTCCTGA TCCGAAAACG TTTTTCGATC

3901 CTTATCCGGC CGGGAACGGT GCATTGGAAC GCGGATTCCC CGTGCCAAGA GTCAGGTAAG TACCGCCTAT AGAGTCTATA GGCCCACCCC CTTGGCTTCG
     GAATAGGCCG GCCCTTGCCA CGTAACCTTG CGCCTAAGGG GCACGGTTCT CAGTCCATTC ATGGCGGATA TCTCAGATAT CCGGGTGGGG GAACCGAAGC

4001 TTAGAACGCG GCTACAATTA ATACATAACC TTTTGGATCG ATCCTACTGA CACTGACATC CACTTTTTCT TTTTCTCCAC AGGTGTCCAC TCCCAGGTCC
     AATCTTGCGC CGATGTTAAT TATGTATTGG AAAACCTAGC TAGGATGACT GTGACTGTAG GTGAAAAAGA AAAAGAGGTG TCCACAGGTG AGGGTCCAGG

4101 AACTGCACCT CGGTTCGCGA AGCTAGCTTG GGCTGCATCG ATTGAATTCC ACCATGGGAT GGTCATGTAT CATCCTTTTT CTAGTAGCAA CTGCAACTGG
     TTGACGTGGA GCCAAGCGCT TCGATCGAAC CCGACGTAGC TAACTTAAGG TGGTACCCTA CCAGTACATA GTAGGAAAAA GATCATCGTT GACGTTGACC
                                                                ^Start LC coding
4201 AGTACATTCA GATATCCAGA TGACCCAGTC CCCGAGCTCC CTGTCCGCCT CTGTGGGCGA TAGGGTCACC ATCACCTGCA AGGCCAGTCA GGATGTGTCT
     TCATGTAAGT CTATAGGTCT ACTGGGTCAG GGGCTCGAGG GACAGGCGGA GACACCCGCT ATCCCAGTGG TAGTGGACGT TCCGGTCAGT CCTACACAGA

4301 ATTGGTGTCG CCTGGTATCA ACAGAAACCA GGAAAAGCTC CGAAACTACT GATTTACTCG GCTTCCTACC GATACACTGG AGTCCCTTCT CGCTTCTCTG
     TAACCACAGC GGACCATAGT TGTCTTTGGT CCTTTTCGAG GCTTTGATGA CTAAATGAGC CGAAGGATGG CTATGTGACC TCAGGGAAGA GCGAAGAGAC

4401 GATCCGGTTC TGGGACGGAT TTCACTCTGA CCATCAGCAG TCTGCAGCCA GAAGACTTCG CAACTTATTA CTGTCAACAA TATTATATTT ATCCTTACAC
     CTAGGCCAAG ACCCTGCCTA AAGTGAGACT GGTAGTCGTC AGACGTCGGT CTTCTGAAGC GTTGAATAAT GACAGTTGTT ATAATATAAA TAGGAATGTG

4501 GTTTGGACAG GGTACCAAGG TGGAGATCAA ACGAACTGTG GCTGCACCAT CTGTCTTCAT CTTCCCGCCA TCTGATGAGC AGTTGAAATC TGGAACTGCT
     CAAACCTGTC CCATGGTTCC ACCTCTAGTT TGCTTGACAC CGACGTGGTA GACAGAAGTA GAAGGGCGGT AGACTACTCG TCAACTTTAG ACCTTGACGA

4601 TCTGTTGTGT GCCTGCTGAA TAACTTCTAT CCCAGAGAGG CCAAAGTACA GTGGAAGGTG GATAACGCCC TCCAATCGGG TAACTCCCAG GAGAGTGTCA
     AGACAACACA CGGACGACTT ATTGAAGATA GGGTCTCTCC GGTTTCATGT CACCTTCCAC CTATTGCGGG AGGTTAGCCC ATTGAGGGTC CTCTCACAGT

4701 CAGAGCAGGA CAGCAAGGAC AGCACCTACA GCCTCAGCAG CACCCTGACG CTGAGCAAAG CAGACTACGA GAAACACAAA GTCTACGCCT GCGAAGTCAC
     GTCTCGTCCT GTCGTTCCTG TCGTGGATGT CGGAGTCGTC GTGGGACTGC GACTCGTTTC GTCTGATGCT CTTTGTGTTT CAGATGCGGA CGCTTCAGTG

4801 CCATCAGGGC CTGAGCTCGC CCGTCACAAA GAGCTTCAAC AGGGGAGAGT GTTAAGCTTC GATGGCCGCC ATGGCCCAAC TTGTTTATTG CAGCTTATAA
     GGTAGTCCCG GACTCGAGCG GGCAGTGTTT CTCGAAGTTG TCCCCTCTCA CAATTCGAAG CTACCGGCGG TACCGGGTTG AACAAATAAC GTCGAATATT

4901 TGGTTACAAA TAAAGCAATA GCATCACAAA TTTCACAAAT AAAGCATTTT TTTCACTGCA TTCTAGTTGT GGTTTGTCCA AACTCATCAA TGTATCTTAT
     ACCAATGTTT ATTTCGTTAT CGTAGTGTTT AAAGTGTTTA TTTCGTAAAA AAAGTGACGT AAGATCAACA CCAAACAGGT TTGAGTAGTT ACATAGAATA

5001 CATGTCTGGA TCGGGAATTA ATTCGGCGCA GCACCATGGC CTGAAATAAG TTTAAACCCT CTGAAAGAGG AACTTGGTTA GGTACCGACT AGTAGCAAGG
     GTACAGACCT AGCCCTTAAT TAAGCCGCGT CGTGGTACCG GACTTTATTC AAATTTGGGA GACTTTCTCC TTGAACCAAT CCATGGCTGA TCATCGTTCC
```

Figure 22C

```
5101 TCGCCACGCA CAAGATCAAT ATTAACAATC AGTCATCTCT CTTTAGCAAT AAAAAGGTGA AAAATTACAT TTTAAAAATG ACACCATAGA CGATGTATGA
     AGCGGTGCGT GTTCTAGTTA TAATTGTTAG TCAGTAGAGA GAAATCGTTA TTTTTCCACT TTTTAATGTA AAATTTTTAC TGTGGTATCT GCTACATACT

5201 AAATAATCTA CTTGGAAATA AATCTAGGCA AAGAAGTGCA AGACTGTTAC CCAGAAAACT TACAAATTGT AAATGAGAGG TTAGTGAAGA TTTAAATGAA
     TTTATTAGAT GAACCTTTAT TTAGATCCGT TTCTTCACGT TCTGACAATG GGTCTTTTGA ATGTTTAACA TTTACTCTCC AATCACTTCT AAATTTACTT

5301 TGAAGATCTA AATAAACTTA TAAATTGTGA GAGAAATTAA TGAATGTCTA AGTTAATGCA GAAACGGAGA GACATACTAT ATTCATGAAC TAAAAGACTT
     ACTTCTAGAT TTATTTGAAT ATTTAACACT CTCTTTAATT ACTTACAGAT TCAATTACGT CTTTGCCTCT CTGTATGATA TAAGTACTTG ATTTTCTGAA

5401 AATATTGTGA AGGTATACTT TCTTTTCACA TAAATTTGTA GTCAATATGT TCACCCCAAA AAAGCTGTTT GTTAACTTGT CAACCTCATT TCAAAATGTA
     TTATAACACT TCCATATGAA AGAAAAGTGT ATTTAAACAT CAGTTATACA AGTGGGGTTT TTTCGACAAA CAATTGAACA GTTGGAGTAA AGTTTTACAT

5501 TATAGAAAGC CCAAAGACAA TAACAAAAAT ATTCTTGTAG AACAAAATGG GAAAGAATGT TCCACTAAAT ATCAAGATTT AGAGCAAAGC ATGAGATGTG
     ATATCTTTCG GGTTTCTGTT ATTGTTTTTA TAAGAACATC TTGTTTTACC CTTTCTTACA AGGTGATTTA TAGTTCTAAA TCTCGTTTCG TACTCTACAC

5601 TGGGGATAGA CAGTGAGGCT GATAAAATAG AGTAGAGCTC AGAAACAGAC CCATTGATAT ATGTAAGTGA CCTATGAAAA AAATATGGCA TTTTACAATG
     ACCCCTATCT GTCACTCCGA CTATTTTATC TCATCTCGAG TCTTTGTCTG GGTAACTATA TACATTCACT GGATACTTTT TTTATACCGT AAAATGTTAC

5701 GGAAAATGAT GATCTTTTTC TTTTTTAGAA AAACAGGGAA ATATATTTAT ATGTAAAAAA TAAAAGGGAA CCCATATGTC ATACCATACA CACAAAAAAA
     CCTTTTACTA CTAGAAAAAG AAAAAATCTT TTTGTCCCTT TATATAAATA TACATTTTTT ATTTTCCCTT GGGTATACAG TATGGTATGT GTGTTTTTTT

5801 TTCCAGTGAA TTATAAGTCT AAATGGAGAA GGCAAAACTT TAAATCTTTT AGAAAATAAT ATAGAAGCAT GCCATCATGA CTTCAGTGTA GAGAAAAATT
     AAGGTCACTT AATATTCAGA TTTACCTCTT CCGTTTTGAA ATTTAGAAAA TCTTTTATTA TATCTTCGTA CGGTAGTACT GAAGTCACAT CTCTTTTTAA

5901 TCTTATGACT CAAAGTCCTA ACCACAAAGA AAAGATTGTT AATTAGATTG CATGAATATT AAGACTTATT TTTAAAATTA AAAAACCATT AAGAAAAGTC
     AGAATACTGA GTTTCAGGAT TGGTGTTTCT TTTCTAACAA TTAATCTAAC GTACTTATAA TTCTGAATAA AAATTTTAAT TTTTTGGTAA TTCTTTTCAG

6001 AGGCCATAGA ATGACAGAAA ATATTTGCAA CACCCCAGTA AAGAGAATTG TAATATGCAG ATTATAAAAA GAAGTCTTAC AAATCAGTAA AAAATAAAAC
     TCCGGTATCT TACTGTCTTT TATAAACGTT GTGGGGTCAT TTCTCTTAAC ATTATACGTC TAATATTTTT CTTCAGAATG TTTAGTCATT TTTTATTTTG

6101 TAGACAAAAA TTTGAACAGA TGAAAGAGAA ACTCTAAATA ATCATTACAC ATGAGAAACT CAATCTCAGA AATCAGAGAA CTATCATTGC ATATACACTA
     ATCTGTTTTT AAACTTGTCT ACTTTCTCTT TGAGATTTAT TAGTAATGTG TACTCTTTGA GTTAGAGTCT TTAGTCTCTT GATAGTAACG TATATGTGAT

6201 AATTAGAGAA ATATTAAAAG GCTAAGTAAC ATCTGTGGCA ATATTGATGG TATATAACCT TGATATGATG TGATGAGAAC AGTACTTTAC CCCATGGGCT
     TTAATCTCTT TATAATTTTC CGATTCATTG TAGACACCGT TATAACTACC ATATATTGGA ACTATACTAC ACTACTCTTG TCATGAAATG GGGTACCCGA

6301 TCCTCCCCAA ACCCTTACCC CAGTATAAAT CATGACAAAT ATACTTTAAA AACCATTACC CTATATCTAA CCAGTACTCC TCAAAACTGT CAAGGTCATC
     AGGAGGGGTT TGGGAATGGG GTCATATTTA GTACTGTTTA TATGAAATTT TTGGTAATGG GATATAGATT GGTCATGAGG AGTTTTGACA GTTCCAGTAG

6401 AAAAATAAGA AAAGTCTGAG GAACTGTCAA AACTAAGAGG AACCCAAGGA GACATGAGAA TTATATGTAA TGTGGCATTC TGAATGAGAT CCCAGAACAG
     TTTTTATTCT TTTCAGACTC CTTGACAGTT TTGATTCTCC TTGGGTTCCT CTGTACTCTT AATATACATT ACACCGTAAG ACTTACTCTA GGGTCTTGTC

6501 AAAAAGAACA GTAGCTAAAA AACTAATGAA ATATAAATAA AGTTTGAACT TTAGTTTTTT TTAAAAAAGA GTAGCATTAA CACGGCAAAG TCATTTTCAT
     TTTTTCTTGT CATCGATTTT TTGATTACTT TATATTTATT TCAAACTTGA AATCAAAAAA AATTTTTTCT CATCGTAATT GTGCCGTTTC AGTAAAAGTA

6601 ATTTTTCTTG AACATTAAGT ACAAGTCTAT AATTAAAAAT TTTTTAAATG TAGTCTGGAA CATTGCCAGA AACAGAAGTA CAGCAGCTAT CTGTGCTGTC
     TAAAAAGAAC TTGTAATTCA TGTTCAGATA TTAATTTTTA AAAAATTTAC ATCAGACCTT GTAACGGTCT TTGTCTTCAT GTCGTCGATA GACACGACAG

6701 GCCTAACTAT CCATAGCTGA TTGGTCTAAA ATGAGATACA TCAACGCTCC TCCATGTTTT TTGTTTTCTT TTTAAATGAA AAACTTTATT TTTTAAGAGG
     CGGATTGATA GGTATCGACT AACCAGATTT TACTCTATGT AGTTGCGAGG AGGTACAAAA AACAAAAGAA AAATTTACTT TTTGAAATAA AAAATTCTCC

6801 AGTTTCAGGT TCATAGCAAA ATTGAGAGGA AGGTACATTC AAGCTGAGGA AGTTTTCCTC TATTCCTAGT TTACTGAGAG ATTGCATCAT GAATGGGTGT
```

Figure 22D

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     TCAAAGTCCA AGTATCGTTT TAACTCTCCT TCCATGTAAG TTCGACTCCT TCAAAAGGAG ATAAGGATCA AATGACTCTC TAACGTAGTA CTTACCCACA

6901 TAAATTTTGT CAAATGCTTT TTCTGTGTCT ATCAATATGA CCATGTGATT TTCTTCTTTA ACCTGTTGAT GGGACAAATT ACGTTAATTG ATTTTCAAAC
     ATTTAAAACA GTTTACGAAA AAGACACAGA TAGTTATACT GGTACACTAA AAGAAGAAAT TGGACAACTA CCCTGTTTAA TGCAATTAAC TAAAAGTTTG

7001 GTTGAACCAC CCTTACATAT CTGGAATAAA TTCTACTTGG TTGTGGTGTA TATTTTTTGA TACATTCTTG GATTCTTTTT GCTAATATTT TGTTGAAAAT
     CAACTTGGTG GGAATGTATA GACCTTATTT AAGATGAACC AACACCACAT ATAAAAAACT ATGTAAGAAC CTAAGAAAAA CGATTATAAA ACAACTTTTA

7101 GTTTGTATCT TTGTTCATGA GAGATATTGG TCTGTTGTTT TCTTTTCTTG TAATGTCATT TTCTAGTTCC GGTATTAAGG TAATGCTGGC CTAGTTGAAT
     CAAACATAGA AACAAGTACT CTCTATAACC AGACAACAAA AGAAAAGAAC ATTACAGTAA AAGATCAAGG CCATAATTCC ATTACGACCG GATCAACTTA

7201 GATTTAGGAA GTATTCCCTC TGCTTCTGTC TTCTGAGGTA CCGCGGCCGC CCGTCGTTTT ACAACGTCGT GACTGGGAAA ACCCTGGCGT TACCCAACTT
     CTAAATCCTT CATAAGGGAG ACGAAGACAG AAGACTCCAT GGCGCCGGCG GGCAGCAAAA TGTTGCAGCA CTGACCCTTT TGGGACCGCA ATGGGTTGAA

7301 AATCGCCTTG CAGCACATCC CCCTTTCGCC AGCTGGCGTA ATAGCGAAGA GGCCCGCACC GATCGCCCTT CCCAACAGTT GCGCAGCCTG AATGGCGAAT
     TTAGCGGAAC GTCGTGTAGG GGGAAAGCGG TCGACCGCAT TATCGCTTCT CCGGGCGTGG CTAGCGGGAA GGGTTGTCAA CGCGTCGGAC TTACCGCTTA

7401 GGCGCCTGAT GCGGTATTTT CTCCTTACGC ATCTGTGCGG TATTTCACAC CGCATACGTC AAAGCAACCA TAGTACGCGC CCTGTAGCGG CGCATTAAGC
     CCGCGGACTA CGCCATAAAA GAGGAATGCG TAGACACGCC ATAAAGTGTG GCGTATGCAG TTTCGTTGGT ATCATGCGCG GGACATCGCC GCGTAATTCG

7501 GCGGCGGGTG TGGTGGTTAC GCGCAGCGTG ACCGCTACAC TTGCCAGCGC CCTAGCGCCC GCTCCTTTCG CTTTCTTCCC TTCCTTTCTC GCCACGTTCG
     CGCCGCCCAC ACCACCAATG CGCGTCGCAC TGGCGATGTG AACGGTCGCG GGATCGCGGG CGAGGAAAGC GAAAGAAGGG AAGGAAAGAG CGGTGCAAGC

7601 CCGGCTTTCC CCGTCAAGCT CTAAATCGGG GGCTCCCTTT AGGGTTCCGA TTTAGTGCTT TACGGCACCT CGACCCCAAA AAACTTGATT TGGGTGATGG
     GGCCGAAAGG GGCAGTTCGA GATTTAGCCC CCGAGGGAAA TCCCAAGGCT AAATCACGAA ATGCCGTGGA GCTGGGGTTT TTTGAACTAA ACCCACTACC

7701 TTCACGTAGT GGGCCATCGC CCTGATAGAC GGTTTTTCGC CCTTTGACGT TGGAGTCCAC GTTCTTTAAT AGTGGACTCT TGTTCCAAAC TGGAACAACA
     AAGTGCATCA CCCGGTAGCG GGACTATCTG CCAAAAAGCG GGAAACTGCA ACCTCAGGTG CAAGAAATTA TCACCTGAGA ACAAGGTTTG ACCTTGTTGT

7801 CTCAACCCTA TCTCGGGCTA TTCTTTTGAT TTATAAGGGA TTTTGCCGAT TTCGGCCTAT TGGTTAAAAA ATGAGCTGAT TTAACAAAAA TTTAACGCGA
     GAGTTGGGAT AGAGCCCGAT AAGAAAACTA AATATTCCCT AAAACGGCTA AAGCCGGATA ACCAATTTTT TACTCGACTA AATTGTTTTT AAATTGCGCT

7901 ATTTTAACAA AATATTAACG TTTACAATTT TATGGTGCAC TCTCAGTACA ATCTGCTCTG ATGCCGCATA GTTAAGCCAG CCCCGACACC CGCCAACACC
     TAAAATTGTT TTATAATTGC AAATGTTAAA ATACCACGTG AGAGTCATGT TAGACGAGAC TACGGCGTAT CAATTCGGTC GGGGCTGTGG GCGGTTGTGG

8001 CGCTGACGCG CCCTGACGGG CTTGTCTGCT CCCGGCATCC GCTTACAGAC AAGCTGTGAC CGTCTCCGGG AGCTGCATGT GTCAGAGGTT TTCACCGTCA
     GCGACTGCGC GGGACTGCCC GAACAGACGA GGGCCGTAGG CGAATGTCTG TTCGACACTG GCAGAGGCCC TCGACGTACA CAGTCTCCAA AAGTGGCAGT

8101 TCACCGAAAC GCGCGAGAGA CGAAAGGGCC TCGTGATACG CCTATTTTTA TAGGTTAATG TCATGATAAT AATGGTTTCT TAGACGTCAG GTGGCACTTT
     AGTGGCTTTG CGCGCTCTCT GCTTTCCCGG AGCACTATGC GGATAAAAAT ATCCAATTAC AGTACTATTA TTACCAAAGA ATCTGCAGTC CACCGTGAAA

8201 TCGGGGAAAT GTGCGCGGAA CCCCTATTTG TTTATTTTTC TAAATACATT CAAATATGTA TCCGCTCATG AGACAATAAC CCTGATAAAT GCTTCAATAA
     AGCCCCTTTA CACGCGCCTT GGGGATAAAC AAATAAAAAG ATTTATGTAA GTTTATACAT AGGCGAGTAC TCTGTTATTG GGACTATTTA CGAAGTTATT

8301 TATTGAAAAA GGAAGAGTAT GAGTATTCAA CATTTCCGTG TCGCCCTTAT TCCCTTTTTT GCGGCATTTT GCCTTCCTGT TTTTGCTCAC CCAGAAACGC
     ATAACTTTTT CCTTCTCATA CTCATAAGTT GTAAAGGCAC AGCGGGAATA AGGGAAAAAA CGCCGTAAAA CGGAAGGACA AAAACGAGTG GGTCTTTGCG

8401 TGGTGAAAGT AAAAGATGCT GAAGATCAGT TGGGTGCACG AGTGGGTTAC ATCGAACTGG ATCTCAACAG CGGTAAGATC CTTGAGAGTT TTCGCCCCGA
     ACCACTTTCA TTTTCTACGA CTTCTAGTCA ACCCACGTGC TCACCCAATG TAGCTTGACC TAGAGTTGTC GCCATTCTAG GAACTCTCAA AAGCGGGGCT

8501 AGAACGTTTT CCAATGATGA GCACTTTTAA AGTTCTGCTA TGTGGCGCGG TATTATCCCG TATTGACGCC GGGCAAGAGC AACTCGGTCG CCGCATACAC
     TCTTGCAAAA GGTTACTACT CGTGAAAATT TCAAGACGAT ACACCGCGCC ATAATAGGGC ATAACTGCGG CCCGTTCTCG TTGAGCCAGC GGCGTATGTG
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Figure 22E

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8601 TATTCTCAGA ATGACTTGGT TGAGTACTCA CCAGTCACAG AAAAGCATCT TACGGATGGC ATGACAGTAA GAGAATTATG CAGTGCTGCC ATAACCATGA
     ATAAGAGTCT TACTGAACCA ACTCATGAGT GGTCAGTGTC TTTTCGTAGA ATGCCTACCG TACTGTCATT CTCTTAATAC GTCACGACGG TATTGGTACT

8701 GTGATAACAC TGCGGCCAAC TTACTTCTGA CAACGATCGG AGGACCGAAG GAGCTAACCG CTTTTTTGCA CAACATGGGG GATCATGTAA CTCGCCTTGA
     CACTATTGTG ACGCCGGTTG AATGAAGACT GTTGCTAGCC TCCTGGCTTC CTCGATTGGC GAAAAAACGT GTTGTACCCC CTAGTACATT GAGCGGAACT

8801 TCGTTGGGAA CCGGAGCTGA ATGAAGCCAT ACCAAACGAC GAGCGTGACA CCACGATGCC TGTAGCAATG GCAACAACGT TGCGCAAACT ATTAACTGGC
     AGCAACCCTT GGCCTCGACT TACTTCGGTA TGGTTTGCTG CTCGCACTGT GGTGCTACGG ACATCGTTAC CGTTGTTGCA ACGCGTTTGA TAATTGACCG

8901 GAACTACTTA CTCTAGCTTC CCGGCAACAA TTAATAGACT GGATGGAGGC GGATAAAGTT GCAGGACCAC TTCTGCGCTC GGCCCTTCCG GCTGGCTGGT
     CTTGATGAAT GAGATCGAAG GGCCGTTGTT AATTATCTGA CCTACCTCCG CCTATTTCAA CGTCCTGGTG AAGACGCGAG CCGGGAAGGC CGACCGACCA

9001 TTATTGCTGA TAAATCTGGA GCCGGTGAGC GTGGGTCTCG CGGTATCATT GCAGCACTGG GGCCAGATGG TAAGCCCTCC CGTATCGTAG TTATCTACAC
     AATAACGACT ATTTAGACCT CGGCCACTCG CACCCAGAGC GCCATAGTAA CGTCGTGACC CCGGTCTACC ATTCGGGAGG GCATAGCATC AATAGATGTG

9101 GACGGGGAGT CAGGCAACTA TGGATGAACG AAATAGACAG ATCGCTGAGA TAGGTGCCTC ACTGATTAAG CATTGGTAAC TGTCAGACCA AGTTTACTCA
     CTGCCCCTCA GTCCGTTGAT ACCTACTTGC TTTATCTGTC TAGCGACTCT ATCCACGGAG TGACTAATTC GTAACCATTG ACAGTCTGGT TCAAATGAGT

9201 TATATACTTT AGATTGATTT AAAACTTCAT TTTTAATTTA AAAGGATCTA GGTGAAGATC CTTTTTGATA ATCTCATGAC CAAAATCCCT TAACGTGAGT
     ATATATGAAA TCTAACTAAA TTTTGAAGTA AAAATTAAAT TTTCCTAGAT CCACTTCTAG GAAAAACTAT TAGAGTACTG GTTTTAGGGA ATTGCACTCA

9301 TTTCGTTCCA CTGAGCGTCA GACCCCGTAG AAAAGATCAA AGGATCTTCT TGAGATCCTT TTTTTCTGCG CGTAATCTGC TGCTTGCAAA CAAAAAAACC
     AAAGCAAGGT GACTCGCAGT CTGGGGCATC TTTTCTAGTT TCCTAGAAGA ACTCTAGGAA AAAAAGACGC GCATTAGACG ACGAACGTTT GTTTTTTTGG

9401 ACCGCTACCA GCGGTGGTTT GTTTGCCGGA TCAAGAGCTA CCAACTCTTT TTCCGAAGGT AACTGGCTTC AGCAGAGCGC AGATACCAAA TACTGTTCTT
     TGGCGATGGT CGCCACCAAA CAAACGGCCT AGTTCTCGAT GGTTGAGAAA AAGGCTTCCA TTGACCGAAG TCGTCTCGCG TCTATGGTTT ATGACAAGAA

9501 CTAGTGTAGC CGTAGTTAGG CCACCACTTC AAGAACTCTG TAGCACCGCC TACATACCTC GCTCTGCTAA TCCTGTTACC AGTGGCTGCT GCCAGTGGCG
     GATCACATCG GCATCAATCC GGTGGTGAAG TTCTTGAGAC ATCGTGGCGG ATGTATGGAG CGAGACGATT AGGACAATGG TCACCGACGA CGGTCACCGC

9601 ATAAGTCGTG TCTTACCGGG TTGGACTCAA GACGATAGTT ACCGGATAAG GCGCAGCGGT CGGGCTGAAC GGGGGGTTCG TGCACACAGC CCAGCTTGGA
     TATTCAGCAC AGAATGGCCC AACCTGAGTT CTGCTATCAA TGGCCTATTC CGCGTCGCCA GCCCGACTTG CCCCCCAAGC ACGTGTGTCG GGTCGAACCT

9701 GCGAACGACC TACACCGAAC TGAGATACCT ACAGCGTGAG CTATGAGAAA GCGCCACGCT TCCCGAAGGG AGAAAGGCGG ACAGGTATCC GGTAAGCGGC
     CGCTTGCTGG ATGTGGCTTG ACTCTATGGA TGTCGCACTC GATACTCTTT CGCGGTGCGA AGGGCTTCCC TCTTTCCGCC TGTCCATAGG CCATTCGCCG

9801 AGGGTCGGAA CAGGAGAGCG CACGAGGGAG CTTCCAGGGG GAAACGCCTG GTATCTTTAT AGTCCTGTCG GGTTTCGCCA CCTCTGACTT GAGCGTCGAT
     TCCCAGCCTT GTCCTCTCGC GTGCTCCCTC GAAGGTCCCC CTTTGCGGAC CATAGAAATA TCAGGACAGC CCAAAGCGGT GGAGACTGAA CTCGCAGCTA

9901 TTTTGTGATG CTCGTCAGGG GGGCGGAGCC TATGGAAAAA CGCCAGCAAC GCGGCCTTTT TACGGTTCCT GGCCTTTTGC TGGCCTTTTG CTCACATGTT
     AAAACACTAC GAGCAGTCCC CCCGCCTCGG ATACCTTTTT GCGGTCGTTG CGCCGGAAAA ATGCCAAGGA CCGGAAAACG ACCGGAAAAC GAGTGTACAA

10001 CTTTCCTGCG TTATCCCCTG ATTCTGTGGA TAACCGTATT ACCGCCTTTG AGTGAGCTGA TACCGCTCGC CGCAGCCGAA CGACCGAGCG CAGCGAGTCA
      GAAAGGACGC AATAGGGGAC TAAGACACCT ATTGGCATAA TGGCGGAAAC TCACTCGACT ATGGCGAGCG GCGTCGGCTT GCTGGCTCGC GTCGCTCAGT

10101 GTGAGCGAGG AAGCGGAAGA GCCCGCGGGC AAGGTCGCCA CGCACAAGAT CAATATTAAC AATCAGTCAT CTCTCTTTAG CAATAAAAAG GTGAAAAATT
      CACTCGCTCC TTCGCCTTCT CGGGCGCCCG TTCCAGCGGT GCGTGTTCTA GTTATAATTG TTAGTCAGTA GAGAGAAATC GTTATTTTTC CACTTTTTAA

10201 ACATTTTAAA AATGACACCA TAGACGATGT ATGAAAATAA TCTACTTGGA AATAAATCTA GGCAAAGAAG TGCAAGACTG TTACCCAGAA AACTTACAAA
      TGTAAAATTT TTACTGTGGT ATCTGCTACA TACTTTTATT AGATGAACCT TTATTTAGAT CCGTTTCTTC ACGTTCTGAC AATGGGTCTT TTGAATGTTT

10301 TTGTAAATGA GAGGTTAGTG AAGATTTAAA TGAATGAAGA TCTAAATAAA CTTATAAATT GTGAGAGAAA TTAATGAATG TCTAAGTTAA TGCAGAAACG
      AACATTTACT CTCCAATCAC TTCTAAATTT ACTTACTTCT AGATTTATTT GAATATTTAA CACTCTCTTT AATTACTTAC AGATTCAATT ACGTCTTTGC
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Figure 22F

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10401 GAGAGACATA CTATATTCAT GAACTAAAAG ACTTAATATT GTGAAGGTAT ACTTTCTTTT CACATAAATT TGTAGTCAAT ATGTTCACCC CAAAAAAGCT
      CTCTCTGTAT GATATAAGTA CTTGATTTTC TGAATTATAA CACTTCCATA TGAAAGAAAA GTGTATTTAA ACATCAGTTA TACAAGTGGG GTTTTTTCGA

10501 GTTTGTTAAC TTGTCAACCT CATTTCAAAA TGTATATAGA AAGCCCAAAG ACAATAACAA AAATATTCTT GTAGAACAAA ATGGGAAAGA ATGTTCCACT
      CAAACAATTG AACAGTTGGA GTAAAGTTTT ACATATATCT TTCGGGTTTC TGTTATTGTT TTTATAAGAA CATCTTGTTT TACCCTTTCT TACAAGGTGA

10601 AAATATCAAG ATTTAGAGCA AAGCATGAGA TGTGTGGGGA TAGACAGTGA GGCTGATAAA ATAGAGTAGA GCTCAGAAAC AGACCCATTG ATATATGTAA
      TTTATAGTTC TAAATCTCGT TTCGTACTCT ACACACCCCT ATCTGTCACT CCGACTATTT TATCTCATCT CGAGTCTTTG TCTGGGTAAC TATATACATT

10701 GTGACCTATG AAAAAAATAT GGCATTTTAC AATGGGAAAA TGATGATCTT TTTCTTTTTT AGAAAAACAG GGAAATATAT TTATATGTAA AAAATAAAAG
      CACTGGATAC TTTTTTTATA CCGTAAAATG TTACCCTTTT ACTACTAGAA AAAGAAAAAA TCTTTTTGTC CCTTTATATA AATATACATT TTTTATTTTC

10801 GGAACCCATA TGTCATACCA TACACACAAA AAAATTCCAG TGAATTATAA GTCTAAATGG AGAAGGCAAA ACTTTAAATC TTTTAGAAAA TAATATAGAA
      CCTTGGGTAT ACAGTATGGT ATGTGTGTTT TTTTAAGGTC ACTTAATATT CAGATTTACC TCTTCCGTTT TGAAATTTAG AAAATCTTTT ATTATATCTT

10901 GCATGCCATC ATGACTTCAG TGTAGAGAAA AATTTCTTAT GACTCAAAGT CCTAACCACA AAGAAAAGAT TGTTAATTAG ATTGCATGAA TATTAAGACT
      CGTACGGTAG TACTGAAGTC ACATCTCTTT TTAAAGAATA CTGAGTTTCA GGATTGGTGT TTCTTTTCTA ACAATTAATC TAACGTACTT ATAATTCTGA

11001 TATTTTTAAA ATTAAAAAAC CATTAAGAAA AGTCAGGCCA TAGAATGACA GAAAATATTT GCAACACCCC AGTAAAGAGA ATTGTAATAT GCAGATTATA
      ATAAAAATTT TAATTTTTTG GTAATTCTTT TCAGTCCGGT ATCTTACTGT CTTTTATAAA CGTTGTGGGG TCATTTCTCT TAACATTATA CGTCTAATAT

11101 AAAAGAAGTC TTACAAATCA GTAAAAAATA AAACTAGACA AAAATTTGAA CAGATGAAAG AGAAACTCTA AATAATCATT ACACATGAGA AACTCAATCT
      TTTTCTTCAG AATGTTTAGT CATTTTTTAT TTTGATCTGT TTTTAAACTT GTCTACTTTC TCTTTGAGAT TTATTAGTAA TGTGTACTCT TTGAGTTAGA

11201 CAGAAATCAG AGAACTATCA TTGCATATAC ACTAAATTAG AGAAATATTA AAAGGCTAAG TAACATCTGT GGCAATATTG ATGGTATATA ACCTTGATAT
      GTCTTTAGTC TCTTGATAGT AACGTATATG TGATTTAATC TCTTTATAAT TTTCCGATTC ATTGTAGACA CCGTTATAAC TACCATATAT TGGAACTATA

11301 GATGTGATGA GAACAGTACT TTACCCCATG GGCTTCCTCC CCAAACCCTT ACCCCAGTAT AAATCATGAC AAATATACTT TAAAAACCAT TACCCTATAT
      CTACACTACT CTTGTCATGA AATGGGGTAC CCGAAGGAGG GGTTTGGGAA TGGGGTCATA TTTAGTACTG TTTATATGAA ATTTTTGGTA ATGGGATATA

11401 CTAACCAGTA CTCCTCAAAA CTGTCAAGGT CATCAAAAAT AAGAAAAGTC TGAGGAACTG TCAAAACTAA GAGGAACCCA AGGAGACATG AGAATTATAT
      GATTGGTCAT GAGGAGTTTT GACAGTTCCA GTAGTTTTTA TTCTTTTCAG ACTCCTTGAC AGTTTTGATT CTCCTTGGGT TCCTCTGTAC TCTTAATATA

11501 GTAATGTGGC ATTCTGAATG AGATCCCAGA ACAGAAAAAG AACAGTAGCT AAAAAACTAA TGAAATATAA ATAAAGTTTG AACTTTAGTT TTTTTTAAAA
      CATTACACCG TAAGACTTAC TCTAGGGTCT TGTCTTTTTC TTGTCATCGA TTTTTTGATT ACTTTATATT TATTTCAAAC TTGAAATCAA AAAAAATTTT

11601 AAGAGTAGCA TTAACACGGC AAAGTCATTT TCATATTTTT CTTGAACATT AAGTACAAGT CTATAATTAA AAATTTTTTA AATGTAGTCT GGAACATTGC
      TTCTCATCGT AATTGTGCCG TTTCAGTAAA AGTATAAAAA GAACTTGTAA TTCATGTTCA GATATTAATT TTTAAAAAAT TTACATCAGA CCTTGTAACG

11701 CAGAAACAGA AGTACAGCAG CTATCTGTGC TGTCGCCTAA CTATCCATAG CTGATTGGTC TAAAATGAGA TACATCAACG CTCCTCCATG TTTTTTGTTT
      GTCTTTGTCT TCATGTCGTC GATAGACACG ACAGCGGATT GATAGGTATC GACTAACCAG ATTTTACTCT ATGTAGTTGC GAGGAGGTAC AAAAAACAAA

11801 TCTTTTTAAA TGAAAAACTT TATTTTTTAA GAGGAGTTTC AGGTTCATAG CAAAATTGAG AGGAAGGTAC ATTCAAGCTG AGGAAGTTTT CCTCTATTCC
      AGAAAAATTT ACTTTTTGAA ATAAAAAATT CTCCTCAAAG TCCAAGTATC GTTTTAACTC TCCTTCCATG TAAGTTCGAC TCCTTCAAAA GGAGATAAGG

11901 TAGTTTACTG AGAGATTGCA TCATGAATGG GTGTTAAATT TTGTCAAATG CTTTTTCTGT GTCTATCAAT ATGACCATGT GATTTTCTTC TTTAACCTGT
      ATCAAATGAC TCTCTAACGT AGTACTTACC CACAATTTAA AACAGTTTAC GAAAAAGACA CAGATAGTTA TACTGGTACA CTAAAAGAAG AAATTGGACA

12001 TGATGGGACA AATTACGTTA ATTGATTTTC AAACGTTGAA CCACCCTTAC ATATCTGGAA TAAATTCTAC TTGGTTGTGG TGTATATTTT TTGATACATT
      ACTACCCTGT TTAATGCAAT TAACTAAAAG TTTGCAACTT GGTGGGAATG TATAGACCTT ATTTAAGATG AACCAACACC ACATATAAAA AACTATGTAA

12101 CTTGGATTCT TTTTGCTAAT ATTTTGTTGA AAATGTTTGT ATCTTTGTTC ATGAGAGATA TTGGTCTGTT GTTTTCTTTT CTTGTAATGT CATTTTCTAG
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Figure 22G

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      GAACCTAAGA AAAACGATTA TAAAACAACT TTTACAAACA TAGAAACAAG TACTCTCTAT AACCAGACAA CAAAAGAAAA GAACATTACA GTAAAAGATC

12201 TTCCGGTATT AAGGTAATGC TGGCCTAGTT GAATGATTTA GGAAGTATTC CCTCTGCTTC TGTCTTCTGA AGCGGAAGAG CGCCCAATAC GCAAACCGCC
      AAGGCCATAA TTCCATTACG ACCGGATCAA CTTACTAAAT CCTTCATAAG GGAGACGAAG ACAGAAGACT TCGCCTTCTC GCGGGTTATG CGTTTGGCGG

12301 TCTCCCCGCG CGTTGGCCGA TTCATTAATG CAGCTGGCAC GACAGGTTTC CCGACTGGAA AGCGGGCAGT GAGCGCAACG CAATTAATGT GAGTTAGCTC
      AGAGGGGCGC GCAACCGGCT AAGTAATTAC GTCGACCGTG CTGTCCAAAG GGCTGACCTT TCGCCCGTCA CTCGCGTTGC GTTAATTACA CTCAATCGAG

12401 ACTCATTAGG CACCCCAGGC TTTACACTTT ATGCTTCCGG CTCGTATGTT GTGTGGAATT GTGAGCGGAT AACAATTTCA CACAGGAAAC AGCTATGACA
      TGAGTAATCC GTGGGGTCCG AAATGTGAAA TACGAAGGCC GAGCATACAA CACACCTTAA CACTCGCCTA TTGTTAAAGT GTGTCCTTTG TCGATACTGT

12501 TGATTACGAA TTAA
      ACTAATGCTT AATT
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>length: 12514

Figure 22H

CMV.PD.1.CMV.2

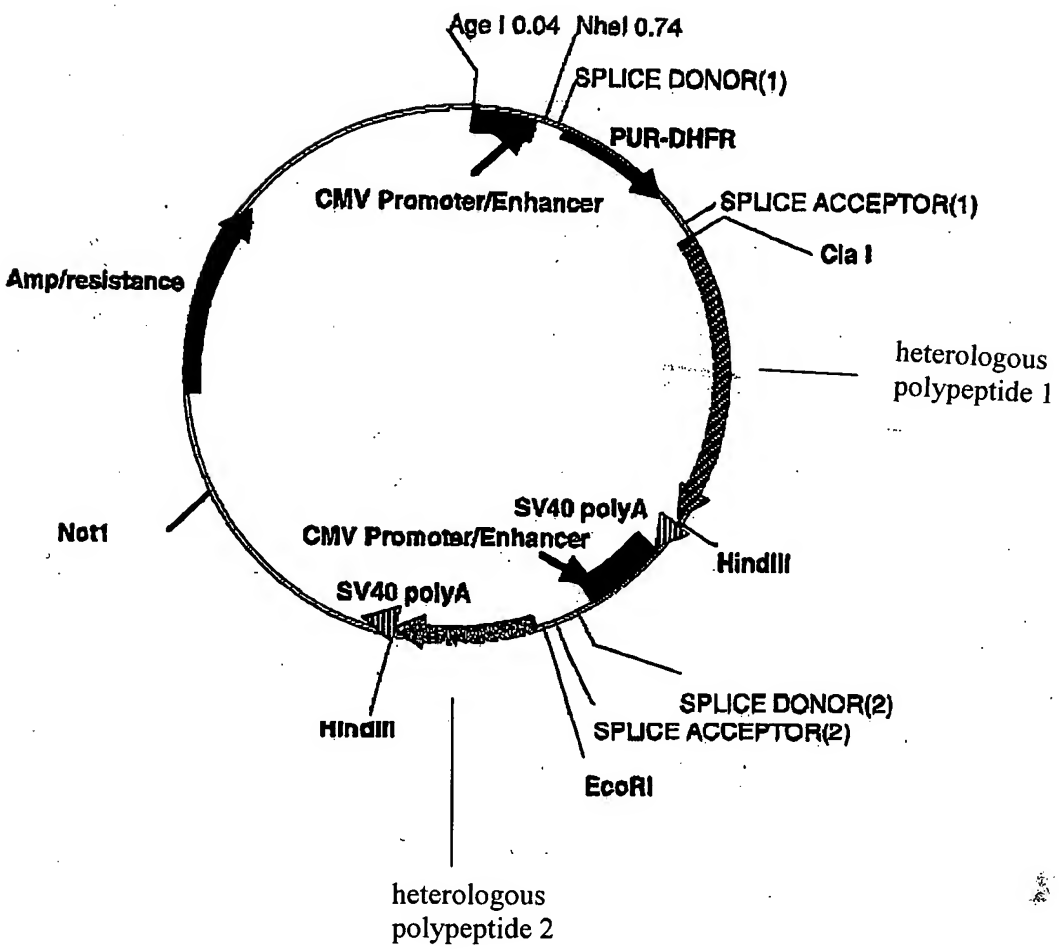

Figure 23

Figure 24A. Plasmid pCMV.IPD.Heterologous polypeptides

5 <400>

60 TTCGAGCTCG CCCGACATTG ATTATTGACT AGAGTCGATC ACCGGTAGTA ATCAATTACG

120 GGGTCATTAG TTCATAGCCC ATATATGGAG TTCCGCGTTA CATAACTTAC GGTAAATGGC

180 CCGCCTGGCT GACCGCCCAA CGACCCCCGC CCATTGACGT CAATAATGAC GTATGTTCCC

240 ATAGTAACGC CAATAGGGAC TTTCCATTGA CGTCAATGGG TGGAGTATTT ACGGTAAACT

300 GCCCACTTGG CAGTACATCA AGTGTATCAT ATGCCAAGTA CGCCCCCTAT TGACGTCAAT

360 GACGGTAAAT GGCCCGCCTG GCATTATGCC CAGTACATGA CCTTATGGGA CTTTCCTACT

420 TGGCAGTACA TCTACGTATT AGTCATCGCT ATTACCATGG TGATGCGGTT TTGGCAGTAC

480 ATCAATGGGC GTGGATAGCG GTTTGACTCA CGGGGATTTC CAAGTCTCCA CCCCATTGAC

540 GTCAATGGGA GTTTGTTTTG GCACCAAAAT CAACGGGACT TTCCAAAATG TCGTAACAAC

600 TCCGCCCCAT TGACGCAAAT GGGCGGTAGG CGTGTACGGT GGGAGGTCTA TATAAGCAGA

660 GCTCGTTTAG TGAACCGTCA GATCGCCTGG AGACGCCATC CACGCTGTTT TGACCTGGGC

720 CCGGCCGAGG CCGCCTCGGC CTCTGAGCTA TTCCAGAAGT AGTGAGGAGG CTTTTTTGGA

780 GGCCTAGGCT TTTGCAAAAA GCTAGCTTAT CCGGCCGGGA ACGGTGCATT GGAACGCGGA

840 TTCCCCGTGC CAAGAGTGAC GTAAGTACCG CCTATAGAGC GACTAGTCCA CCATGACCGA

900 GTACAAGCCC ACGGTGCGCC TCGCCACCCG CGACGACGTC CCGCGGGCCG TACGCACCCT

960 CGCCGCCGCG TTCGCCGACT ACCCCGCCAC GCGCCACACC GTAGACCCGG ACCGCCACAT

1020 CGAGCGGGTC ACCGAGCTGC AAGAACTCTT CCTCACGCGC GTCGGGCTCG ACATCGGCAA

1080 GGTGTGGGTC GCGGACGACG GCGCCGCGGT GGCGGTCTGG ACCACGCCGG AGAGCGTCGA

1140 AGCGGGGGCG GTGTTCGCCG AGATCGGCCC GCGCATGGCC GAGTTGAGCG GTTCCCGGCT

1200 GGCCGCGCAG CAACAGATGG AAGGCCTCCT GGCGCCGCAC CGGCCCAAGG AGCCCGCGTG

1260 GTTCCTGGCC ACCGTCGGCG TCTCGCCCGA CCACCAGGGC AAGGGTCTGG GCAGCGCCGT

1320 CGTGCTCCCC GGAGTGGAGG CGGCCGAGCG CGCCGGGGTG CCCGCCTTCC TGGAGACCTC

1380 CGCGCCCCGC AACCTCCCCT TCTACGAGCG GCTCGGCTTC ACCGTCACCG CCGACGTCGA

1440 GGTGCCCGAA GGACCGCGCA CCTGGTGCAT GACCCGCAAG CCCGGTGCCA ACATGGTTCG

Figure 24B

1500 ACCATTGAAC TGCATCGTCG CCGTGTCCCA AAATATGGGG ATTGGCAAGA ACGGAGACCT

1560 ACCCTGGCCT CCGCTCAGGA ACGCGTTCAA GTACTTCCAA AGAATGACCA CAACCTCTTC

1620 AGTGGAAGGT AAACAGAATC TGGTGATTAT GGGTAGGAAA ACCTGGTTCT CCATTCCTGA

1680 GAAGAATCGA CCTTTAAAGG ACAGAATTAA TATAGTTCTC AGTAGAGAAC TCAAAGAACC

1740 ACCACGAGGA GCTCATTTTC TTGCCAAAAG TTTGGATGAT GCCTTAAGAC TTATTGAACA

1800 ACCGGAATTG GCAAGTAAAG TAGACATGGT TTGGATAGTC GGAGGCAGTT CTGTTTACCA

1860 GGAAGCCATG AATCAACCAG GCCACCTCAG ACTCTTTGTG ACAAGGATCA TGCAGGAATT

1920 TGAAAGTGAC ACGTTTTTCC CAGAAATTGA TTTGGGGAAA TATAAACCTC TCCCAGAATA

1980 CCCAGGCGTC CTCTCTGAGG TCCAGGAGGA AAAAGGCATC AAGTATAAGT TTGAAGTCTA

2040 CGAGAAGAAA GACTAACGTT AACTGCTCCC CTCCTAAAGC TATGCATTTT TATAAGACCA

2100 TGAGACTTTT GCTGGCTTTA GATCCCCTTG GCTTCGTTAG AACGCAGCTA CAATTAATAC

2160 ATAACCTTAT GTATCATACA CATACGATTT AGGTGACACT ATAGAATAAC ATCCACTTTG

2220 CCTTTCTCTC CACAGGTGTC CACTCCCAGG TCCAACTGCA CCTCGGTTCT ATCGATTGAA

2280 TTCCACC <from 2287 to 3736, insertion site for a selected heterologous polypeptide>

3737 CGA TGGCCGCCAT GGCCCAACTT GTTTATTGCA GCTTATAATG

3780 GTTACAAATA AAGCAATAGC ATCACAAATT TCACAAATAA AGCATTTTTT TCACTGCATT

3840 CTAGTTGTGG TTTGTCCAAA CTCATCAATG TATCTTATCA TGTCTGGATC GGGAATTAAT

3900 TCGGCGCAGC ACCATGGCCT GAAATAACCT CTGAAAGAGG AACTTGGTTA GGTACCTATT

3960 AATAGTAATC AATTACGGGG TCATTAGTTC ATAGCCCATA TATGGAGTTC CGCGTTACAT

4020 AACTTACGGT AAATGGCCCG CCTGGCTGAC CGCCCAACGA CCCCCGCCCA TTGACGTCAA

4080 TAATGACGTA TGTTCCCATA GTAACGCCAA TAGGGACTTT CCATTGACGT CAATGGGTGG

4140 AGTATTTACG GTAAACTGCC CACTTGGCAG TACATCAAGT GTATCATATG CCAAGTACGC

4200 CCCCTATTGA CGTCAATGAC GGTAAATGGC CCGCCTGGCA TTATGCCCAG TACATGACCT

4260 TATGGGACTT TCCTACTTGG CAGTACATCT ACGTATTAGT CATCGCTATT ACCATGGTGA

Figure 24C

4320 TGCGGTTTTG GCAGTACATC AATGGGCGTG GATAGCGGTT TGACTCACGG GGATTTCCAA

4380 GTCTCCACCC CATTGACGTC AATGGGAGTT TGTTTTGGCA CCAAAATCAA CGGGACTTTC

4440 CAAAATGTCG TAACAACTCC GCCCCATTGA CGCAAATGGG CGGTAGGCGT GTACGGTGGG

4500 AGGTCTATAT AAGCAGAGCT CGTTTAGTGA ACCGTCAGAT CGCCTGGAGA CGCCATCCAC

4560 GCTGTTTTGA CCTGCTAGCT TATCCGGCCG GGAACGGTGC ATTGGAACGC GGATTCCCCG

4620 TGCCAAGAGT CAGGTAAGTA CCGCCTATAG AGTCTATAGG CCCACCCCCT TGGCTTCGTT

4680 AGAACGCGGC TACAATTAAT ACATAACCTT TTGGATCGAT CCTACTGACA CTGACATCCA

4740 CTTTTTCTTT TTCTCCACAG GTGTCCACTC CCAGGTCCAA CTGCACCTCG GTTCGCGAAG

4800 CTCGCTTGGG CTGCATCGAT TGAATTCCAC C <from 4831 to 5533, insertion site for a selected heterologous polypeptide>

5534 CGATGG CCGCCATGGC CCAACTTGTT TATTGCAGCT TATAATGGTT

5580 ACAAATAAAG CAATAGCATC ACAAATTTCA CAAATAAAGC ATTTTTTTCA CTGCATTCTA

5640 GTTGTGGTTT GTCCAAACTC ATCAATGTAT CTTATCATGT CTGGATCGGG AATTAATTCG

5700 GCGCAGCACC ATGGCCTGAA ATAAGTTTAA ACCCTCTGAA AGAGGAACTT GGTTAGGTAC

5760 CGACTAGTCT TTTGCAAAAA GCTGTTACCT CGAGCGGCCG CTTAATTAAG GCGCGCCATT

5820 TAAATCCTGC AGGTAACAGC TTGGCACTGG CCGTCGTTTT ACAACGTCGT GACTGGGAAA

5880 ACCCTGGCGT TACCCAACTT AATCGCCTTG CAGCACATCC CCCTTTCGCC AGCTGGCGTA

5940 ATAGCGAAGA GGCCCGCACC GATCGCCCTT CCCAACAGTT GCGCAGCCTG AATGGCGAAT

6000 GGCGCCTGAT GCGGTATTTT CTCCTTACGC ATCTGTGCGG TATTTCACAC CGCATACGTC

6060 AAAGCAACCA TAGTACGCGC CCTGTAGCGG CGCATTAAGC GCGGCGGGTG TGGTGGTTAC

6120 GCGCAGCGTG ACCGCTACAC TTGCCAGCGC CCTAGCGCCC GCTCCTTTCG CTTTCTTCCC

6180 TTCCTTTCTC GCCACGTTCG CCGGCTTTCC CCGTCAAGCT CTAAATCGGG GGCTCCCTTT

6240 AGGGTTCCGA TTTAGTGCTT TACGGCACCT CGACCCCAAA AAACTTGATT TGGGTGATGG

6300 TTCACGTAGT GGGCCATCGC CCTGATAGAC GGTTTTTCGC CCTTTGACGT TGGAGTCCAC

6360 GTTCTTTAAT AGTGGACTCT TGTTCCAAAC TGGAACAACA CTCAACCCTA TCTCGGGCTA

6420 TTCTTTTGAT TTATAAGGGA TTTTGCCGAT TTCGGCCTAT TGGTTAAAAA ATGAGCTGAT

Figure 24D

6480 TTAACAAAAA TTTAACGCGA ATTTTAACAA AATATTAACG TTTACAATTT TATGGTGCAC

6540 TCTCAGTACA ATCTGCTCTG ATGCCGCATA GTTAAGCCAG CCCCGACACC GCCCCGACAC

6600 CCGCCAACAC CCGCTGACGC GCCCTGACGG GCTTGTCTGC TCCCGGCATC CGCTTACAGA

6660 CAAGCTGTGA CCGTCTCCGG GAGCTGCATG TGTCAGAGGT TTTCACCGTC ATCACCGAAA

6720 CGCGCGAGAG ACGAAAGGGC CTCGTGATAC GCCTATTTTT ATAGGTTAAT GTCATGATAA

6780 TAATGGTTTC TTAGACGTCA GGTGGCACTT TTCGGGGAAA TGTGCGCGGA ACCCCTATTT

6840 GTTTATTTTT CTAAATACAT TCAAATATGT ATCCGCTCAT GAGACAATAA CCCTGATAAA

6900 TGCTTCAATA ATATTGAAAA AGGAAGAGTA TGAGTATTCA ACATTTCCGT GTCGCCCTTA

6960 TTCCCTTTTT TGCGGCATTT TGCCTTCCTG TTTTTGCTCA CCCAGAAACG CTGGTGAAAG

7020 TAAAAGATGC TGAAGATCAG TTGGGTGCAC GAGTGGGTTA CATCGAACTG GATCTCAACA

7080 GCGGTAAGAT CCTTGAGAGT TTTCGCCCCG AAGAACGTTT TCCAATGATG AGCACTTTTA

7140 AAGTTCTGCT ATGTGGCGCG GTATTATCCC GTATTGACGC CGGGCAAGAG CAACTCGGTC

7200 GCCGCATACA CTATTCTCAG AATGACTTGG TTGAGTACTC ACCAGTCACA GAAAAGCATC

7260 TTACGGATGG CATGACAGTA AGAGAATTAT GCAGTGCTGC CATAACCATG AGTGATAACA

7320 CTGCGGCCAA CTTACTTCTG ACAACGATCG GAGGACCGAA GGAGCTAACC GCTTTTTTGC

7380 ACAACATGGG GGATCATGTA ACTCGCCTTG ATCGTTGGGA ACCGGAGCTG AATGAAGCCA

7440 TACCAAACGA CGAGCGTGAC ACCACGATGC CTGTAGCAAT GGCAACAACG TTGCGCAAAC

7500 TATTAACTGG CGAACTACTT ACTCTAGCTT CCCGGCAACA ATTAATAGAC TGGATGGAGG

7560 CGGATAAAGT TGCAGGACCA CTTCTGCGCT CGGCCCTTCC GGCTGGCTGG TTTATTGCTG

7620 ATAAATCTGG AGCCGGTGAG CGTGGGTCTC GCGGTATCAT TGCAGCACTG GGGCCAGATG

7680 GTAAGCCCTC CCGTATCGTA GTTATCTACA CGACGGGGAG TCAGGCAACT ATGGATGAAC

7740 GAAATAGACA GATCGCTGAG ATAGGTGCCT CACTGATTAA GCATTGGTAA CTGTCAGACC

7800 AAGTTTACTC ATATATACTT TAGATTGATT TAAAACTTCA TTTTTAATTT AAAAGGATCT

7860 AGGTGAAGAT CCTTTTTGAT AATCTCATGA CCAAAATCCC TTAACGTGAG TTTTCGTTCC

7920 ACTGAGCGTC AGACCCCGTA GAAAAGATCA AAGGATCTTC TTGAGATCCT TTTTTTCTGC

Figure 24E

7980 GCGTAATCTG CTGCTTGCAA ACAAAAAAAC CACCGCTACC AGCGGTGGTT TGTTTGCCGG

8040 ATCAAGAGCT ACCAACTCTT TTTCCGAAGG TAACTGGCTT CAGCAGAGCG CAGATACCAA

8100 ATACTGTTCT TCTAGTGTAG CCGTAGTTAG GCCACCACTT CAAGAACTCT GTAGCACCGC

8160 CTACATACCT CGCTCTGCTA ATCCTGTTAC CAGTGGCTGC TGCCAGTGGC GATAAGTCGT

8220 GTCTTACCGG GTTGGACTCA AGACGATAGT TACCGGATAA GGCGCAGCGG TCGGGCTGAA

8280 CGGGGGGTTC GTGCACACAG CCCAGCTTGG AGCGAACGAC CTACACCGAA CTGAGATACC

8340 TACAGCGTGA GCTATGAGAA AGCGCCACGC TTCCCGAAGG GAGAAAGGCG GACAGGTATC

8400 CGGTAAGCGG CAGGGTCGGA ACAGGAGAGC GCACGAGGGA GCTTCCAGGG GGAAACGCCT

8460 GGTATCTTTA TAGTCCTGTC GGGTTTCGCC ACCTCTGACT TGAGCGTCGA TTTTTGTGAT

8520 GCTCGTCAGG GGGGCGGAGC CTATGGAAAA ACGCCAGCAA CGCGGCCTTT TTACGGTTCC

8580 TGGCCTTTTG CTGGCCTTTT GCTCACATGT TCTTTCCTGC GTTATCCCCT GATTCTGTGG

8640 ATAACCGTAT TACCGCCTTT GAGTGAGCTG ATACCGCTCG CCGCAGCCGA ACGACCGAGC

8700 GCAGCGAGTC AGTGAGCGAG GAAGCGGAAG AGCGCCCAAT ACGCAAACCG CCTCTCCCCG

8760 CGCGTTGGCC GATTCATTAA TGCAGCTGGC ACGACAGGTT TCCCGACTGG AAAGCGGGCA

8820 GTGAGCGCAA CGCAATTAAT GTGAGTTAGC TCACTCATTA GGCACCCCAG GCTTTACACT

8880 TTATGCTTCC GGCTCGTATG TTGTGTGGAA TTGTGAGCGG ATAACAATTT CACACAGGAA

8906 ACAGCTATGA CATGATTACG AATTAA